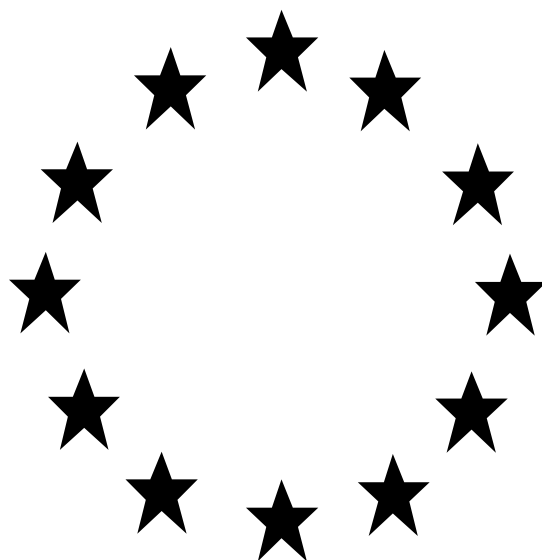




Draft Assessment Report (DAR)

- public version -

**Initial risk assessment provided by the rapporteur Member State
The Netherlands for the existing active substance**

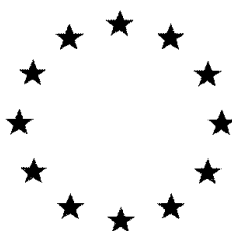
PYRIDABEN

**of the third stage (part B) of the review programme
referred to in Article 8(2) of Council Directive 91/414/EEC**

Volume 3, Annex B, part 1, B.1 – B.5

August 2007

European Commission



VOLUME 3 **Annex B**

Rapporteur Member State: The Netherlands

March 2007

Draft Assessment Report and Proposed Decision of the Netherlands prepared in the context of the possible inclusion of pyridaben in Annex I of Council Directive 91/414/EEC

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B.1 Identity**B.1.1 Identity of active substance (Annex IIA 1 and 3.1)**

All points of Annex IIA, Section I are addressed in Volume 1, Level 1.

B.1.2 Identity of the plant protection product (Annex IIIA 1)

All points of Annex IIIA, Section 1 are addressed in Volume 1, Level 1.

B.1.3 References relied on

Documents M-II and M-III, Pyridaben and Nexter Pro, Nissan Chemical Industries Ltd.

B.2 Physical and chemical properties**B.2.1 Physical and chemical properties of the active substance (Annex IIA 2)**

See Table B.2.1-01.

B.2.2 Physical, chemical and technical properties of the plant protection product (Annex IIIA 2)

See Table B.2.2-01.

Table B.2.1-01 Summary of the physical and chemical properties of the active substance (studies were conducted under GLP and completed to an acceptable standard and results were considered to be valid unless specified otherwise).

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.1 (IIA 2.1)	Melting point	100.0%	OECD 102, capillary/liquid bath method.	109.4 to 110.6°C		Hirai, 2000
B.2.1.1 (IIA 2.1)	Melting point	Tech. a.s. 98.3%	EPA D 63.5	107.9 to 109.6°C		South, 1992
B.2.1.2 (IIA 2.1)	Boiling point	100.0%	OECD 113, TG/DTA	Thermal decomposition was observed before boiling occurred (see section B.2.1.3).	Method complies with EEC A.2	Hirai, 2000
B.2.1.3 (IIA 2.1)	Thermal stability	100.0%	OECD 113, TG/DTA	Exothermic processes and mass loss from 200°C to 400°C (thermal degradation and elimination of volatile decomposition products).		Hirai, 2000
B.2.1.4 (IIA 2.2)	Relative density	100.0%	OECD 109, air comparison pycnometer.	Relative density: 1.201		Hirai, 2000
B.2.1.4 (IIA 2.2)	Relative density	Tech. a.s. 98.3%	EPA D 63.7, Gay- Lussac pycnometer.	Density: 1.204 g/cm ³ at 25°C		South, 1992
B.2.1.5 (IIA 2.3)	Vapour pressure	98%	Guideline not specified, evaporation rate determination.	<1x10 ⁻⁷ mbar at 52.7°C (equivalent to <1x10 ⁻⁵ Pa, calculated by RMS)	No loss of weight over 33 hours at 52.7°C. Method is based on the effusion method (EEC A.4 and OECD 104). Method acceptable.	Gückel, 1992

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.5 (IIA 2.3)	Vapour pressure	Not specified	EEC A.4, calculation method	2.5×10^{-4} Pa at 20°C 5.3×10^{-4} Pa at 25°C	The vapour pressure was calculated using an experimentally determined boiling temperature of 185.0°C at reduced pressure (2 mm Hg). This theoretical value is considered to be not relevant since an experimentally determined value is available.	Schuurman, 1986

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.6 (IIA 2.3)	Volatility, Henry's law constant		Calculation.	$<3 \times 10^{-1} \text{ Pa} \cdot \text{m}^3 \cdot \text{mol}^{-1}$	Not GLP. A vapour pressure of $<1 \times 10^{-5} \text{ Pa}$ (determined at 53°C) and a water solubility of $1.2 \times 10^{-2} \text{ mg/L}$ (at 24°C) were used to calculate the Henry's law constant. The water solubility is found to be unacceptable and should be determined under GLP according to EEC A.6 and OECD 105. Therefore, the result for Henry's Law constant is provisional pending submission of new data on water solubility. A new water solubility study is in progress. When final a new calculation of the Henry's low constant will be performed.	Oki, 2000
B.2.1.7 (IIA 2.4)	Appearance: physical state	100.0%	Visual assessment.	Crystalline solid (23.6°C)	Not GLP.	Ogi, 2000
B.2.1.7 (IIA 2.4)	Appearance: physical state	Tech. a.s. 98.3%	EPA D 63.3, visual assessment.	Crystalline powder (25°C)		South, 1992
B.2.1.8 (IIA 2.4)	Appearance: colour	100.0%	Visual assessment, chroma meter.	White (23.6°C; Munsell 6.8B 9.2/0.0 (V/C)).	Not GLP.	Ogi, 2000

section (Annex point)	study	purity	method	results	comment	reference																														
B.2.1.8 (IIA 2.4)	Appearance: colour	Tech. a.s. 98.3%	EPA D 63.2, visual assessment.	White (25°C)		South, 1992																														
B.2.1.9 (IIA 2.4)	Appearance: odour	100.0%	Olfactory assessment.	No detectable odour (23.6°C)	Not GLP.	Ogi, 2000																														
B.2.1.9 (IIA 2.4)	Appearance: odour	Tech. a.s. 98.3%	EPA D 63.4, olfactory assessment.	Odourless (25°C)		South, 1992																														
B.2.1.10 (IIA 2.5)	Spectra	100.0%	UV/Vis: OECD 101 IR, NMR and MS: standard methodology.	UV/Vis-spectrum: neutral, acidic and basic solutions in methanol at 24.2°C. <table><tr><th>Medium / Concentra- tion (mol/L)/pH</th><th>Absorban- ce maxima (nm)</th><th>Molar absorption coefficient (L/(molxcmm))</th></tr><tr><td>Neutral / 5.654x10⁻⁵</td><td>296.5</td><td>11746</td></tr><tr><td></td><td>236.2</td><td>21102</td></tr><tr><td></td><td>223.4</td><td>23221</td></tr><tr><td>Acidic / 5.654x10⁻⁵</td><td>296.9</td><td>11785</td></tr><tr><td></td><td>236.3</td><td>21142</td></tr><tr><td></td><td>223.3</td><td>23327</td></tr><tr><td>Basic / 5.654x10⁻⁵</td><td>296.6</td><td>11724</td></tr><tr><td></td><td>236.3</td><td>21015</td></tr><tr><td></td><td>223.2</td><td>23037</td></tr></table>	Medium / Concentra- tion (mol/L)/pH	Absorban- ce maxima (nm)	Molar absorption coefficient (L/(molxcmm))	Neutral / 5.654x10 ⁻⁵	296.5	11746		236.2	21102		223.4	23221	Acidic / 5.654x10 ⁻⁵	296.9	11785		236.3	21142		223.3	23327	Basic / 5.654x10 ⁻⁵	296.6	11724		236.3	21015		223.2	23037		Ogi, 2000
Medium / Concentra- tion (mol/L)/pH	Absorban- ce maxima (nm)	Molar absorption coefficient (L/(molxcmm))																																		
Neutral / 5.654x10 ⁻⁵	296.5	11746																																		
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	236.3	21015																																		
	223.2	23037																																		

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section (Annex point)	study	purity	method	results	comment	reference
B.2.1.11 (IIA 2.6)	Solubility in water	99.6%	Guideline not specified, column elution method.	0.012 mg/L in distilled water at 24°C	Not GLP, performed in 1986 (predated to GLP). Method is based on but does not comply with EEC A.6. At a flow rate of 60 mL/hr three samples were taken, whose concentration did not differ more than about 27% in a random fashion (upper acceptable guideline limit: $\pm 30\%$). The average concentration was determined to be the water solubility. According to the guideline five successive samples should be taken whose concentration should not differ more than 30% and a second run at half the flow rate of the first (i.e. 60 mL/hr x 0.5 = 30 mL/hr) should be performed. Halving the flow rate must continue until two successive runs give the same solubility. The water solubility under GLP according to EEC A.6 and OECD 105 should be determined. Study in progress.	Etoh, 1987

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.12 (IIA 2.7)	Solubility in organic solvents	Tech. a.s. 98.3%	OECD 105	Solubility at 20°C: xylene: 345 g/L dichloromethane: >1000 g/L acetone: 333 g/L ethyl acetate: 305 g/L.	<0.1 mg/l very slightly soluble 0.1-10 slightly soluble 10-1000 moderately soluble >1000 readily soluble	Hirai, 2000
B.2.1.12 (IIA 2.7)	Solubility in organic solvents	Tech. a.s. 98.3%	EPA D 63.8	Solubility at 25°C: acetonitrile: 95.2 g/L 1-octanol: 71.1 g/L methanol: 49.4 g/L n-hexane: 14.1 g/L.	<0.1 mg/l very slightly soluble 0.1-10 slightly soluble 10-1000 moderately soluble >1000 readily soluble	South, 1992
B.2.1.13 (IIA 2.8)	Partition co- efficient	99.6%	OECD 107, flask-shaking method.	Log P _{ow} at 23°C: >6.37	Not GLP, performed in 1987 (predated to GLP).	Etoh, 1987
B.2.1.15 (IIA 2.9)	Hydrolysis rate	Pyrida- ben C ¹⁴ , purity 99.18%	EPA N:161.1	No hydrolytic degradation after 30 days incubation at pH 5.0, pH 7.0 and pH 9.0 at 25°C.		O'Connor, 1992

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.16 (IIA 2.9)	Photochemical degradation	[benzene -U-14C]- pyridabe n: radio chemical purity ≥97.4%; [pyridazin one-3,6- 14C]- pyridabe n: radio chemical purity ≥96.6%	EPA N:161-2.	Under test conditions (Xenon light, 425 W/m ²), the DT50 (photolysis, 25°C) for pyridaben is 6.8 minutes. Major photodegradates were W-1 (max. 27.9% AR, DT50 <1.5 hours) and B-3 (max. 27.2% AR, photolytically stable).		O'Connor, 1995
B.2.1.16 (IIA 2.9)	Photochemical degradation	[benzene -U-14C]- pyridabe n: radio chemical purity ≥99.28%; [pyridazin one-3,6- 14C]- pyridabe n: radio chemical purity ≥98.57%	EPA N:161-2.	After 360 hours, CO ₂ major photodegradate (10.6% AR).		O'Connor, 1997

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section (Annex point)	study	purity	method	results	comment	reference
B.2.1.17 (IIA 2.9)	Quantum yield	99.2% radiochemical purity	SETAC (1995)	Quantum yield of pyridaben: 0.0304 mole/Einstein.		Crowe, 2002
B.2.1.18 (IIA 2.9)	Dissociation constant (pKa)	Not relevant	Statement	Not applicable, pyridaben does not dissociate.	Due to low water solubility, determination of the pKa by tests recommended in the guideline (OECD 112) is not practically feasible. However, it is accepted that pyridaben does not dissociate in the environmentally relevant pH range of 4 to 9 (pKa estimated by RMS using Pcalc version 5.0 (module in PALLAS version 3.0) was -3.60).	Document M-II

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.19 (IIA 2.10)	Stability in air, photochemical oxidative degradation	Not relevant	Atkinson calculation	Half-life based on a hydroxyl radical concentration of 9.7×10^5 OH/cm ³ : 4.8 hours.	The reported half-life in air based on reaction with hydroxyl radicals (assuming a concentration in the atmosphere of 1.5×10^6 OH radicals/cm ³) was 3.1 hours. The employed OH radical concentration of 1.5×10^6 OH radicals/cm ³ has been revised by Atkinson. The half-life, recalculated by the RMS using a OH radical concentration of $9.7 \times$ 10^5 molecule/cm ³ , was 4.8 hours.	Comb, 2000
B.2.1.20 (IIA 2.11)	Flammability and auto-flammability (technical active substance)	Not specified	EEC A.10 EEC A.13	A.10, flammability: not flammable. A.13, pyrophoric properties; not pyrophoric.	Purity test substance not reported (data to be provided). A new study for the flammability is in progress.	Schuurman, 1986
B.2.1.20 (IIA 2.11)	Flammability and auto-flammability (technical active substance)	Tech. a.s. 98.3%	EPA D 63.16	No auto-ignition up to 475°C.		Schweitzer, 1992
B.2.1.21 (IIA 2.12)	Flash point (technical active substance)			Not applicable for solids.		

section (Annex point)	study	purity	method	results	comment	reference
B.2.1.22 (IIA 2.13)	Explosive properties (technical active substance)	Not specified	EEC A.14	Pyridaben does not explode under the effect of a flame, is not sensitive to shock but was sensitive to friction. Conclusion, pyridaben has explosive properties under the conditions of this test.	Purity test substance not reported (data to be provided).	Schuurman, 1991
B.2.1.22 (IIA 2.13)	Explosive properties (technical active substance)	Tech. a.s. 98.3%	EPA D 63.16, shock sensitivity, TGA analysis.	Not sensitive to shock. Thermally stable and not thermally explosive.		Schweitzer, 1992
B.2.1.22 (IIA 2.13)	Explosive properties (technical active substance)	Not specified	UN, Recommendations on the Transport of Dangerous Goods	TNO 50/70 Tube Test: no detonation. Time Pressure Test: minimum pressure not reached. Deflagration Test: neither ignition nor deflagration.	Purity test substance not reported. As this study is no data requirement, no additional data need to be provided. A new study for the explosive properties is in progress to show that pyridaben is not explosive	Schuurman, 1991
B.2.1.23 (IIA 2.15)	Oxidising properties (technical active substance)	Tech. a.s. 99.2%	EEC A.17	No oxidizing properties.		Comb, 2001
B.2.1.24 (IIA 2.14)	Surface tension	Not relevant	Statement	Not applicable since the water solubility is below 1 mg/L (i.e. 0.012 mg/L).		Document M-II

Table B.2.2-01 Summary of the physical and chemical properties of the plant protection product

Product name: Pyridaben 75WP in WSB; with 750 g/kg Pyridaben (studies were conducted with pyridaben 75WP without WSB, under GLP and completed to an acceptable standard and results were considered to be valid, unless specified otherwise).

section (Annex point)	study	method	results	comment	reference
B.2.2.1 (IIIA 2.1)	Appearance: physical state	EPA 63.3, visual assessment.	Fine powder (at 25°C).		Fersch, 1991
B.2.2.1 (IIIA 2.1)	Appearance: physical state	Visual assessment.	Powder.		Kastel, 1996
B.2.2.1 (IIIA 2.1)	Appearance: physical state	Visual assessment.	Very fine powder at 20°C.		Comb, 2001
B.2.2.2 (IIIA 2.1)	Appearance: colour	EPA 63.2, visual assessment.	Tan (at room temperature; 22 to 24°C).		Fersch, 1991
B.2.2.2 (IIIA 2.1)	Appearance: colour	Visual assessment.	Light beige.		Kastel, 1996
B.2.2.2 (IIIA 2.1)	Appearance: colour	Visual assessment.	Light grey (5YR 8/1 on Munsell Color system)		Comb, 2001
B.2.2.3 (IIIA 2.1)	Appearance: odour	EPA 63.4, olfactory assessment.	Faint burnt or vanilla (at room temperature; 22 to 24°C).		Fersch, 1991
B.2.2.3 (IIIA 2.1)	Appearance: odour	Olfactory assessment.	Faint aromatic.		Kastel, 1996
B.2.2.3 (IIIA 2.1)	Appearance: odour	Olfactory assessment.	Faint odour of clay.		Comb, 2001

section (Annex point)	study	method	results	comment	reference
B.2.2.4 (IIIA 2.2)	Explosive properties	Statement.	Neither the active ingredient nor any of the formulation inerts are explosive according to the information on current Material Safety Data Sheets.	Not acceptable , an expert statement should be based on the structural formula of each component and not on the information on MSDS's.	Fersch, 1991
B.2.2.4 (IIIA 2.2)	Explosive properties	EEC A.14, friction, shock and Koenen test.	Not explosive		Comb, 2001
B.2.2.5 (IIIA 2.2)	Oxidising properties	EEC A.17	Not oxidizing.		Comb, 2001
B.2.2.5 (IIIA 2.2)	Oxidising properties	EPA 63-14, calorimetry	A strong exothermic reaction was observed with the powerful oxidant KMnO_4 and a less exothermic reaction with the less powerful oxidant KBrO_3 . A very slow exothermic reaction was observed (no significant rapid reaction was observed, but a slight increase in baseline slope) when mixed with reducing agents zinc or iron and mildly endothermic reactions (indicating dissolution/dispersion) were observed when mixed with water or CO_2 .	Pyridaben 75WP may be considered to be a reducing agent, and should not be mixed with or stored in proximity to oxidizers.	Kinnaird, 1992
B.2.2.5 (IIIA 2.2)	Oxidising properties	EPA 63-20, corrosive characteristics ASTM D 638- 89	Storage in HDPE containers at 50°C for 100 days resulted in a yellow discoloration. No other visual differences were noted. Storage did not significantly (<1%) alter the tensile strength at yield (ASTM Test method for tensile properties of plastics) of the containers.		Sweetapple, 1992

section (Annex point)	study	method	results	comment	reference
B.2.2.6 (IIIA 2.3)	Flammability	EEC A.10EEC method A 10, A 11 or A 12	Not flammable.		Comb, 2001
B.2.2.6 (IIIA 2.3)	Flammability	EEC A.10EEC method A 10, A 11 or A 12	Not flammable.		Löffler, 1996
B.2.2.7 (IIIA 2.3)	Auto-flammability	EEC A.16EEC method A 15 or A 16 or UN- Bowes- Cameron- Cage-Test	No self-ignition temperature below 400° C.		Comb, 2001
B.2.2.7 (IIIA 2.3)	Auto-flammability	EEC A.16EEC method A 15 or A 16 or UN- Bowes- Cameron- Cage-Test	No self-ignition temperature below 400° C.		Löffler, 1996
B.2.2.8 (IIIA 2.3)	Flash point		Not required for a WP formulationsolids diluted for use		
B.2.2.9 (IIIA 2.4)	Acidity/alkalinity		Not required since the formulation is not acidic and neither alkaline.		
B.2.2.10 (IIIA 2.4)	pH	EPA 63.12CIPAC MT 75	pH of 1% dispersion at 25°C: 8.7 to 8.8Where relevant, pH of 1% aqueous dilution, emulsion or dispersion		Fersch, 1991
B.2.2.10 (IIIA 2.4)	pH	CIPAC MT 75CIPAC MT 75	1.0% dispersion in CIPAC water D: 7.9 0.1% dispersion in CIPAC water D: 7.1 1.0% dispersion in water: 8.5 0.1% dispersion in water: 7.4 (measurements at room temperature)Where relevant, pH of 1% aqueous dilution, emulsion or dispersion		Kastel, 1996

section (Annex point)	study	method	results	comment	reference
B.2.2.10 (IIIA 2.4)	pH	CIPAC MT 75	1% w/v suspension in water: pH 8.7 1% w/v suspension in CIPAC water D: 8.1		Comb, 2001
B.2.2.11 (IIIA 2.5)	Surface tension	EEC A.5 EEC method A 5	55.3 mN/m (0.1% dispersion; 20°C) 41.3 mN/m (1.0% dispersion; 20°C) liquids % suspension = 40.5 mN/m		Kastel, 1996
B.2.2.12 (IIIA 2.5)	Viscosity		Not required for a WP formulation solids diluted for use		
B.2.2.13 (IIIA 2.6)	Relative density	EEC A.3	D ₄ ²⁰ : 1.299 liquids		Kastel, 1996
B.2.2.14 (IIIA 2.6)	Bulk (tap) density	EPA 63.7	Free fall: 0.22 g/mL Packed: 0.25 g/mL		Fersch, 1991
B.2.2.14 (IIIA 2.6)	Bulk (tap) density	CIPAC MT 33	Tapped: 0.25 g/mL		Comb, 2001
B.2.2.14 (IIIA 2.6)	Bulk (tap) density	CIPAC MT 33	Loose: 0.248 g/mL Tapped: 0.260 g/mL		Kastel, 1996
B.2.2.14 (IIIA 2.7)	Storage stability	CIPAC MT 46	The content of pyridaben did not change significantly after storage for 14 days in a glass beaker at 54°C under a pressure of 25 g/cm ² .	Further information demonstrating the physical stability of the preparation is given in the next two studies.	Kastel, 1996
B.2.2.14 (IIIA 2.7)	Storage stability	EPA 63-17	The content of pyridaben did not change significantly after storage for 98 days at 50°C and after storage for 12 months at 25°C. Samples were stored in 4 oz high density polyethylene bottles. The wet time at study initiation and after 12 months of storage did not change significantly. The suspensibility after 14 months storage was 91.9%.		Yeh, 1993

section (Annex point)	study	method	results	comment	reference
B.2.2.14 (IIIA 2.7)	Storage stability	CIPAC MT 46 CIPAC MT 75 CIPAC MT 53 CIPAC MT 47 CIPAC MT 15 CIPAC MT 59 OECD 110 CIPAC MT 176	Pyridaben 75WP is chemically and physically stable when stored at 40°C for 8 weeks in commercial sachets. The test substance packaging (WSB) did not show any signs of damage following the storage interval. Properties determined prior to and following storage: active substance (% w/w pyridaben), appearance, pH (1% w/v), wettability, persistent foaming, suspensibility (0.012 and 0.2% w/v), wet sieving (75 µm), particle size distribution, dissolution rate of water soluble bags, stability of packaging (visual).	Dissolution rate of water soluble bags: bags did not fully dissolve and blocked the test funnel. Notifier will submit a sprayability test to show that the formulation with the water-soluble bag is no problem in practice.	Comb, 2001
B.2.2.15 (IIIA 2.7)	Shelf life	CIPAC MT 75 CIPAC MT 53 CIPAC MT 47 CIPAC MT 15 CIPAC MT 59 OECD 110 CIPAC MT 176	Pyridaben 75WP is chemically and physically stable when stored for two years under ambient conditions in commercial sachets. The test substance packaging (WSB) did not show any signs of damage following the storage interval. Properties determined prior to and after 6, 12, 18 and 24 months storage: active substance (% w/w pyridaben), appearance, pH (1% w/v), wettability, persistent foaming, suspensibility (0.012 and 0.2% w/v), wet sieving (75 µm), particle size distribution, dissolution rate of water soluble bags, stability of packaging (visual). If <2 years, shelf life in months at appropriate temps. required	Study agreed with GCPF Technical Monograph No. 17. Dissolution rate of water soluble bags: bags did not fully dissolve and blocked the test funnel. Notifier will submit a sprayability test to show that the formulation with the water-soluble bag is no problem in practice.	Comb, 2003

section (Annex point)	study	method	results	comment	reference
B.2.2.15 (IIIA 2.7)	Shelf life	EPA 63-17 and 63-20	Compatible with large (114 g) and small (14 g) Monosol 8030 PVA bags with paper/Kard-O-Gard (KOG) as outer barrier bags. No degradation of packaging or active ingredient occurred after storage for 2 years in commercial type packaging. If <2 years, shelf life in months at appropriate temps. required	According to document M-III the primary packaging is PVA and the outer packaging is corrugated, double wall, fibreboard. The tested packaging is identical to the reported commercial packaging in Document M-III.	Sotack, 1998
B.2.2.16 (IIIA 2.8)	Wettability	CIPAC MT 53	75 seconds using CIPAC water D.	The wettability (75 s) slightly exceeded the trigger of 60 s. Normally the formulation shall be wetted in 1 minute, otherwise, evidence must be submitted demonstrating acceptable wetting in the spray tank or other application equipment. However, several tests (section 2.2.14, 2.2.15 and 2.2.16) were conducted showing a wettability <1 minute.	Kastel, 1996
B.2.2.16 (IIIA 2.8)	Wettability	CIPAC MT 53	40 seconds using CIPAC water D.		Comb, 2001
B.2.2.17 (IIIA 2.8)	Persistent foaming	ASTM-D 1173/53 CIPAC MT 47	1.0% at room temperature. Foam immediately: 75 mm Foam after 1 min: 70 mm Foam after 3, 5 and 15 min: 55 mm 1.0% at room temperature. Foam after 1 min: 1.3 mL Foam after 15 min: 0 mL	The amount of foam produced during the performance of the ASTM test is in accordance with the test result obtained with CIPAC MT 47.	Kastel, 1996

section (Annex point)	study	method	results	comment	reference
B.2.2.17 (IIIA 2.8)	Persistent foaming	CIPAC MT 47	0.2% w/v dilution in CIPAC water D: 7 mL foam after 1 minute. The test was performed using a solution of the preparation and the WSB in the same ratio as in the recommended application concentration.		Comb, 2001
B.2.2.18 (IIIA 2.8)	Suspensibility	CIPAC MT 15.1	Concentration: 1.0% in CIPAC water D Suspensibility: 97% Suspensibility after storage for 14 days at 54°C under a pressure of 25 g/cm ² : 95% water dispersible solid products (e.g. WP, WDG or SC)		Kastel, 1996
B.2.2.18 (IIIA 2.8)	Suspensibility	CIPAC MT 15.1	96.4% at 0.012% w/v in CIPAC water D 95.3% at 0.2% w/v in CIPAC water D. The test was performed using a solution of the preparation and the WSB in the same ratio as in the recommended application concentration.	The concentrations tested encompass the practical in use concentration.	Comb, 2001
B.2.2.19 (IIIA 2.8)	Suspension stability Spontaneity		Not required for a WP formulation.		
B.2.2.20 (IIIA 2.8)	Dilution stability		Not required for a WP formulation.		
B.2.2.21 (IIIA 2.8)	Dry sieve test	CIPAC Method MT 59.1	Not required for a WP formulation.solids diluted for use		
B.2.2.22 (IIIA 2.8)	Wet sieve test	CIPAC MT 59.3	Residue on 200 µm sieve: 0% Residue on 100 µm sieve: 0% Residue on 45 µm sieve: 0%		Kastel, 1996
B.2.2.22 (IIIA 2.8)	Wet sieve test	CIPAC MT 59.3	Residue on 75 µm sieve: 0.03% w/w. The test was performed using a solution of the preparation and the WSB in the same ratio as in the recommended application concentration.		Comb, 2001

section (Annex point)	study	method	results	comment	reference
B.2.2.23 (IIIA 2.8)	Particle size distribution	Laser Diffraction OECD Method 110	Particle size of suspended test sample in water at room temperature: Particle size ≤10%: ≤0.8 µm (d10%) Medium particle size: 2.9 µm (d50%) Particle size ≤10%: ≥7.7 µm (d90%).		Kastel, 1996
B.2.2.23 (IIIA 2.8)	Particle size distribution	CIPAC MT 58.3 or MT 170 OECD 110, image analysis OECD Method 110	77% by mass <10 µm Mass median diameter: ca. 5 µm		Comb, 2001
B.2.2.24 (IIIA 2.8)	Content of dust/fines	CIPAC MT 58.3 or MT 170 CIPAC Method MT 171 or OECD Method 110	Not required for a WP formulation.solids diluted for use	GLP	
B.2.2.25 (IIIA 2.8)	Attrition and friability	CIPAC MT 176	Not required for a WP formulation.solids diluted for use		
B.2.2.26 (IIIA 2.8)	Emulsifiability, re- emulsifiability and emulsion stability		Not required for a WP formulation.solids diluted for use		
B.2.2.27 (IIIA 2.8)	Stability of dilute emulsion		Not required for a WP formulation.solids diluted for use		
B.2.2.28 (IIIA 2.8)	Flowability	CIPAC Method MT 172	Not required for a WP formulation.solids diluted for use		

section (Annex point)	study	method	results	comment	reference
B.2.2.29 (IIIA 2.8)	Pourability (rinsibility)		Not required for a WP formulation.solids diluted for use		
B.2.2.30 (IIIA 2.8)	Dustability	CIPAC Method MT 34	Not required for a WP formulation.solids diluted for use		
B.2.2.31 (IIIA 2.8)	Adherence and distribution to seeds	CIPAC Method MT 175	Not intended for use for seed treatment.solids diluted for use		
2.9.1	Physical compatibility with other products	Static and dynamic tank mix compatibility.	In all tests Pyridaben 75WP was added first. Benlate 50WP, Guthion 2L, Micro-Mix-N-2-Way, Rubigan EC and Urea: compatible with slight-heavy agitation, may require antifoam agent. Basicop, COC, Kocide 101 and Kocide 606: compatible with slight-heavy agitation, should not remain static for >24 h. Bayleton 50 DF and Nova 40W: compatible with slight-heavy agitation, should not remain static for >24 h, may require antifoam agent. Captan 50W, Imidan 50W, Lorsban 4E, Micro-Mix-N-4-Way, Micro-Mix-Z-M, Morestan 25WP, Rally 40W, Sevin 80S and Supracide 2E: compatible with slight-heavy agitation. Supreme oil and Agrimycin 17: Not compatible. Kryocide WP: Compatible by static tank mix alone.	Not GLP.	Fornes, 1993
2.9.1	Physical compatibility with other products	Static and dynamic tank mix compatibility.	Compatible with agitation: Growers 435 Soluble Oil, Growers 455 Soluble Oil, 435 Soluble Oil, 455 Soluble Oil, Helena Sol-Oil 97 (435), Helena Sol-Oil 97 (455),	Not GLP. No data required as no mixing is proposed.	Byrne, 1995

section (Annex point)	study	method	results	comment	reference
			Helena 435, 435 Soluble Oil-MicroFlo, 455 Soluble Oil-MicroFlo, Sunspray Ultrafine Spray Oil, Sunspray 7N, Volck Oil, Amag Citrus Oil and Ultraphos 24 (0-24-0). Compatible with agitation and defoamer required: Nu-Film, Superior Miscible Spray Oil, Regulaid, LI700 and Nutra Spray Zinc-50. Compatible, however does not suspend well, defoamer required: Mora Leaf Plus (15-15-12).		
2.9.2	Chemical compatibility with other products	Statement	There was no chemical reaction observed.	No analytical evidence was provided for this statement. No data required as no mixing is proposed.	Document M-III.
	Dissolution rate water soluble bag	CIPAC MT 176	Bags did not fully dissolve and blocked test funnel.	Bags may block filter or nozzles of application equipment. Notifier will submit a sprayability test to show that the formulation with the water-soluble bag is no problem in practice.	Comb, 2001
	Dissolution rate water soluble bag	CIPAC MT 176	Mean flow time: 9 seconds. Traces of the bag on the 250 µm sieve.	Not GLP.	Kastel, 2001

B.2.3 Summary of physical and chemical properties

B.2.3.1 Active substance

Physical and chemical properties of the active substance

Pyridaben pure is a white crystalline solid at room temperature with a melting temperature of 109.4 to 110.6°C. Thermal decomposition starts at 200°C and the vapour pressure was determined to be $<1 \times 10^{-5}$ Pa at 25°C. Pyridaben Technical is a white crystalline powder. The (technical) substance is not flammable nor autoflammable and has no oxidizing properties. Pyridaben is sensitive to friction and is considered to present a danger of explosion (however a new study on explosive properties is in progress). The log Pow at 23°C is >6.37 . Pyridaben is hydrolytically stable under typical environmental conditions (pH 5.0, 7.0 and 9.0) and does not dissociate. Its quantum yield is 0.0304 and the DT50 for photolysis in water during irradiation with Xenon light is 6.8 minutes.

The following data is not available or was considered to be insufficiently reliable and should be provided:

- The water solubility under GLP according to EEC A.6 and OECD 105 should be determined and a new Henry constant calculated.
- The report on the determination of flammability is to be supplemented with data on the purity of the substance.
- The report on the determination of explosive properties is to be supplemented with data on the purity of the substance.

B.2.3.2 Plant protection product

Pyridaben 75WP in WSB (750 g/kg Pyridaben) is a tan, light beige/grey fine powder. The product is not flammable not autoflammable and has neither explosive properties nor oxidizing properties. The pH of a 1% dispersion is 8.7 to 8.8. An accelerated storage test of 14 days at 54°C, 8 weeks at 40°C and 98 days at 50°C, a shelf-life study of 1 year at 25°C and 2 years at ambient conditions have determined the physico-chemical stability of the product.

The following data is not available and should be provided:

- Bags did not fully dissolve and blocked the test funnel in three out of four tests. A practical sprayability test showing acceptable dissolution in a spray tank must be performed (Study is in progress).

B.2.4 References relied on**References for the active substance**

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIA, 2.1.1	Hirai, Y.	2000	Pyridaben: Melting point of the purified active substance Nissan Chemical Industries, Ltd., Report no. P31 GLP, Unpublished	Y	NCI
IIA, 2.1.1	South, L. P.	1992	Physical characterization of Pyridaben (Determination of color, physical state, odor, melting point, bulk density, and pH) Battelle Nissan Chemical Industries, Ltd. Report no. P17 GLP, Unpublished	Y	NCI
IIA, 2.1.2/3	Hirai, Y.	2000	Pyridaben: Thermal Stability of the Purified Active Substance	Y	NCI
IIA, 2.2	Hirai, Y.	2000	Pyridaben: Density of the purified active substance Nissan Chemical Industries, Ltd. Report no. P33 GLP, Unpublished	Y	NCI
IIA, 2.2	South, L. P.	1992	Physical characterization of Pyridaben (Determination of color, physical state, odor, melting point, bulk density, and pH) Battelle Nissan Chemical Industries, Ltd. Report no. P17 GLP, Unpublished	Y	NCI
IIA, 2.3.1	Gückel, Dr.	1992	Physical properties report - Vapor pressure determination for Pyridaben BASF Aktiengesellschaft Report no. P37 GLP, Unpublished	Y	BASF
IIA, 2.4.1/01	Ogi, N.	2000	Pyridaben: Colour, physical state and odour of the purified active substance Nissan Chemical Industries, Ltd. Report no. P34 Non-GLP, Unpublished	Y	NCI
IIA, 2.4.1/02	South, L. P.	1992	Physical characterization of Pyridaben (Determination of color, physical state, odor, melting point, bulk density, and pH) Battelle Nissan Chemical Industries, Ltd. Report no. P17 GLP, Unpublished	Y	NCI
IIA, 2.4.2/01	Ogi, N.	2000	Pyridaben: Colour, physical state and odour of the purified active substance Nissan Chemical Industries, Ltd. Report no. P34 Non-GLP, Unpublished	Y	NCI

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IIA, 2.4.2/02	South, L. P.	1992	Physical characterization of Pyridaben (Determination of color, physical state, odor, melting point, bulk density, and pH) Battelle Nissan Chemical Industries, Ltd. Report no. P17 GLP, Unpublished	Y	NCI
IIA, 2.5.1	Ogi, N.	2000	Pyridaben: Spectra of the purified active substance Nissan Chemical Industries, Ltd. Report no. P35 GLP, Unpublished	Y	NCI
IIA, 2.7/01	Hirai, Y.	2000	Pyridaben: Solubility in organic solvents Nissan Chemical Industries, Ltd. Report no. P36 GLP, Unpublished	Y	NCI
IIA, 2.7/02	South, L. P.	1992	Determination of solubility of Pyridaben Battelle Nissan Chemical Industries, Ltd. Report no. P18 GLP, Unpublished	Y	NCI
IIA, 2.8	Etoh, C.	1987	Partition coefficient of NC-129 Chemical Biotesting Center, Nissan Chemical Industries, Ltd. Report no. P8 Non-GLP, Unpublished	Y	NCI
IIA, 2.9.1	O'Connor, J.	1992	NC-129: Determination of hydrolysis as a function of pH Life Science Research Ltd. Nissan Chemical Industries, Ltd. Report no. M26 GLP, Unpublished	Y	NCI
IIA, 2.9.2/01	O'Connor, J.	1995	NC-129: Photodegradation in water Pharmaco LSR Ltd. Nissan Chemical Industries, Ltd. Report no. M33 GLP, Unpublished	Y	NCI
IIA, 2.9.2/02	O'Connor, J.	1997	Determination of the photodegradation of NC-129 in water (supplementary study) Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. M34 GLP, Unpublished	Y	NCI
IIA, 2.9.2/03	Crowe, A.	2002	Pyridaben: Determination of Quantum yield Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P41 GLP, Unpublished	Y	NCI
IIA, 2.9.3	Crowe, A.	2002	Pyridaben: Determination of Quantum yield Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P41 GLP, Unpublished	Y	NCI

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIA, 2.10	Comb, A.L.	2000	Pyridaben photochemical oxidative degradation in air Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P39 GLP, Unpublished	Y	NCI
IIA, 2.11.1	Schuurman, P.	1986	Physico-chemical properties of NCI 834084 Prins Maurits Laboratorium TNO Nissan Chemical Industries, Ltd. Report no. P12 GLP, Unpublished	Y	NCI
IIA, 2.11.2	Schweitzer, M. G.	1992	Determination of the explosive properties of Pyridaben Battelle Nissan Chemical Industries, Ltd. Report no. P22 GLP, Unpublished	Y	NCI
IIA, 2.13/01	Schuurman, P.	1986	Physico-chemical properties of NCI 834084 Prins Maurits Laboratorium TNO Nissan Chemical Industries, Ltd. Report no. P12 GLP, Unpublished	Y	NCI
IIA, 2.13/02	Schuurman, P.	1987	Deflagration and detonation properties of NCI 834084 Prins Maurits Laboratorium TNO Nissan Chemical Industries, Ltd. Report no. P13 GLP, Unpublished	Y	NCI
IIA, 2.13/03	Schweitzer, M. G.	1992	Determination of the explosive properties of Pyridaben Battelle Nissan Chemical Industries, Ltd. Report no. P22 GLP, Unpublished	Y	NCI
IIA, 2.15	Comb, A. L.	2001	Pyridaben: Oxidising properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P40 GLP, Unpublished	Y	NCI

References for the plant protection product

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIIA, 2.1/01	Fersch, K. E.	1991	Determination of the pH, color, physical state, odor, explosability, and bulk density of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P2WP75 GLP, Unpublished	Y	BASF
IIIA, 2.1/02	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.1/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.1/04	Fersch, K. E.	1991	Determination of the pH, color, physical state, odor, explosability, and bulk density of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P2WP75 GLP, Unpublished	Y	BASF
IIIA, 2.1/05	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.1/06	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.1/07	Fersch, K. E.	1991	Determination of the pH, color, physical state, odor, explosability, and bulk density of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P2WP75 GLP, Unpublished	Y	BASF
IIIA, 2.1/08	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIIA, 2.1/09	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.2.1/01	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.2.2/01	Kinnaird, M.; Vanhook, C.	1992	Determination of oxidizing or reducing action of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P3WP75 GLP, Unpublished	Y	BASF
IIIA, 2.2.2/02	Sweetapple, G. G.	1992	Pyridaben 300 11 I – Determination of corrosion characteristics Ricerca, Inc. BASF Aktiengesellschaft Report no P5WP75 GLP, Unpublished	Y	BASF
IIIA, 2.2.2/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.3/02	Löffler	1996	Safety characteristics of the crop protection product BAS 300 11 I BASF Aktiengesellschaft Report no. P10WP75 GLP, Unpublished	Y	BASF
IIIA, 2.3/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.3/04	Löffler	1996	Safety characteristics of the crop protection product BAS 300 11 I BASF Aktiengesellschaft Report no. P10WP75 GLP, Unpublished	Y	BASF
IIIA, 2.3/05	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI

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IIIA, 2.4.2/01	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.4.2/02	Fersch, K. E.	1991	Determination of the pH, color, physical state, odor, explosability, and bulk density of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P2WP75 GLP, Unpublished	Y	BASF
IIIA, 2.4.2/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.5.3	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.6.1	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.6.2/01	Fersch, K. E.	1991	Determination of the pH, color, physical state, odor, explosability, and bulk density of BAS 300 11 I BASF Corporation BASF Aktiengesellschaft Report no. P2WP75 GLP, Unpublished	Y	BASF
IIIA, 2.6.2/02	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.6.2/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.7.1/01	Yeh, L. T.	1993	BAS 300 11 I – Determination of storage stability Ricerca, Inc. BASF Aktiengesellschaft Report no. P27 GLP, Unpublished	Y	BASF

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IIIA, 2.7.1/02	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.7.1/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Accelerated storage stability Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P18WP75 GLP, Unpublished	Y	NCI
IIIA, 2.7.3/01	Comb, A. L.	2003	Pyridaben 75 WP (BAS 300 19 I): Storage stability Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P19WP75 GLP, Unpublished	Y	NCI
IIIA, 2.7.3/02	Sotack, G. S.	1998	BAS 300 I: Storage stability and corrosion evaluation of a Pyridaben insecticide formulation in commercial-type packages BASF Corporation BASF Aktiengesellschaft Report no. P12-3WP75 GLP, Unpublished	Y	BASF
IIIA, 2.7.3/03	Kastel, R.	2001	Dissolution rate of water soluble bag of the formulation BAS 300 19 I (Nexter Por) BASF Aktiengesellschaft Report no. P20WP75 Non-GLP, Unpublished	Y	BASF
IIIA, 2.8.1/01	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.8.1/02	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.8.2/01	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.8.2/02	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIIA, 2.8.2/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.8.3/01	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.8.3/02	Yeh, L. T.	1993	BAS 300 11 I – Determination of storage stability Ricerca, Inc. BASF Aktiengesellschaft Report no. P27 GLP, Unpublished	Y	BASF
IIIA, 2.8.3/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.8.5/02	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.8.5/03	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.8.6.1/01	Kastel, R.	1996	Physical and chemical properties report for Sanmite (BAS 300 11 I) BASF Aktiengesellschaft Report no. P8WP75 GLP, Unpublished	Y	BASF
IIIA, 2.8.6.1/02	Comb, A. L.	2001	Pyridaben 75 WP (BAS 300 19 I): Physico-chemical properties Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P17WP75 GLP, Unpublished	Y	NCI
IIIA, 2.9.1/01	Fomes, W. L., Byrne, T.	1993	BAS 300 11 I Tank mix compatibility study BASF Corporation BASF Aktiengesellschaft Report no. P15WP75 Non-GLP, Unpublished	Y	BASF

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
IIIA, 2.9.1/02	Byrne, T.	1995	Compatibility of BAS 300 11 I with various crop oils and fertilizers BASF Corporation BASF Aktiengesellschaft Report no. P16WP75 Non-GLP, Unpublished	Y	BASF

B.3 Data on application and further information

B.3.1 Data on application relevant to the active substance (Annex IIA 3.1 to 3.6)

B.3.1.1 Function (Annex IIA 3.1)

Pyridaben is an insecticide and acaricide.

B.3.1.2 Effects on harmful organisms (Annex IIA 3.2.1)

Pyridaben is orally and/or percutaneously taken into mobile forms of insects (whiteflies, aphids, mites). Pyridaben rapidly paralyzes and kills the pests within 24 hours when treated at concentrations for practical uses. In addition, pyridaben quickly stops the embryonic development of whiteflies/mites and kills embryos when treated on eggs.

B.3.1.3 Translocation in plants (Annex IIA 3.2.2)

Pyridaben is not translocated in plants.

B.3.1.4 Fields of use (Annex IIA 3.3)

Pyridaben is used in the field on citrus and in glass-houses on tomato.

B.3.1.5 Pests controlled and crops protected (Annex IIA 3.4.1, 3.4.2)

Pyridaben controls the following insects and mites on citrus orchards and greenhouse tomatoes:

- citrus: *Panonychus* sp., *Tetranychus urticae*, *Tetranychus cinnarinus*, *Trialeurodes vaporariorum*, *Frankliniella occidentalis*, *Typhlocyba rosae*;
- tomato: *Spodoptera esigua*; *Tetranychus* sp., *Trialeurodes vaporariorum*, *Bemisia tabaci*.

B.3.1.6 Mode of action (Annex IIA 3.5.1)

Pyridaben inhibits the mitochondrial electron transport. It was shown in *in vitro* studies that pyridaben inhibits mitochondrial respiration by acting on the electron transport chain on the inner membrane of mitochondria and the acting site was on the Complex I, NADH-CoQ reductase (IC₅₀ value was 10⁻⁸M). Experimental *in vivo* experiments strongly suggest that the inhibition of Complex I is the exact mode of action of pyridaben's mitocidal and possibly insecticidal activity. Further experiments revealed that the PSST unit of Complex I is involved in the respiratory inhibiting activity and therefore its mitocidal and insecticidal activity.

B.3.1.7 Information relative to the formation of active metabolites or degradation products (Annex IIA 3.5.2, 3.5.3)

There are no known active metabolites or degradation products to which the active substance must be converted to exert its intended effect.

B.3.1.8 Information on the possible occurrence of the development of resistance or cross-resistance (Annex IIA 3.6)

Up till now considering the observations made over last years, it can be concluded that pyridaben represents a moderate risk for resistance development. Appropriate resistance management strategies for pyridaben have already been implemented following IRAC recommendations.

B.3.2 Data on application relevant to the plant protection product (Annex IIIA 3)

Product name: Nexter Pro (Pyridaben 75 WP in WSB)

B.3.2.1 Field of use (Annex IIIA 3.1)

Intended for agricultural use in the field (citrus) and in glasshouse (tomato).

B.3.2.2 Nature of the effects on harmful organisms (Annex IIIA 3.2)

Pyridaben is orally or percutaneously taken into mobile insects or mites.

B.3.2.3 Pests controlled and crops protected (Annex IIIA 3.3)

Pyridaben controls the following insects and mites on citrus orchards and greenhouse tomatoes:

- citrus: *Panonychus* sp, *Tetranychus urticae*, *Tetranychus cinnarinus*, *Trialeurodes vaporariorum*, *Frankliniella occidentalis*, *Typhlocyba rosae*;
- tomato: *Spodoptera esigua*; *Tetranychus* sp., *Trialeurodes vaporariorum*, *Bemisia tabaci*.

Rate of application (Annex IIIA 3.4)

Nexter Pro is intended to be used as an insecticide on:

- citrus will be applied as 400 g undiluted product per ha (300 g a.s./ha). Per ha 750 – 6000 L water is used. The diluted product contains 0.0067 – 0.053 kg product per hectoliter water which is equivalent to 0.005 – 0.04 kg a.s. per hectoliter water (0.05 – 0.4 g a.s./L).
- tomato will be applied as 333.3 g undiluted product per ha (250 g a.s./ha). Per ha 625 – 5000 L water is used. The diluted product contains 0.0067 – 0.053 kg product per hectoliter water which is equivalent to 0.005 – 0.04 kg a.s. per hectoliter water (0.05 – 0.4 g a.s./L).

Concentration of active substance in material used (Annex IIIA 3.5)

Nexter Pro is an WP formulation containing 750 g/kg of pure pyridaben.

Description of the method of application, type of equipment used and type and volume of diluent per unit of area or volume (Annex IIIA 3.6)

Nexter Pro is intended to be used on:

- citrus and will be applied tractor mounted with trailed broadcast air assisted sprayer (i.e. mist blower, motor pump spray gun, high pressure rotary sprayer). As a diluent water is used, normally 1000 L water per ha is used (range: 750 – 6000 L per ha);
- greenhouse tomatoes and will be applied by various hydraulic sprayers (i.e. backpack and knapsack sprayers). As a diluent water is used, normally 1250 L water per ha is used (range: 625 – 5000 L per ha).

Number and timing of applications and duration of protection afforded (Annex IIIA 3.7)

Citrus:

Nexter Pro will be applied at infestation (no later than BBCH 83). The duration of protection afforded by each application is a rapid knock down application and has a long residual activity.

Tomato:

Nexter Pro will be applied at infestation (no later than BBCH 89). The duration of protection afforded by each application is a rapid knock down application and has a long residual activity.

B.3.2.4 Minimum waiting periods or other precautions between last application and sowing or planting of succeeding crops. Limitations on choice of succeeding crops (Annex IIIA 3.8)

It is not necessary to define waiting periods, since crop rotation is not relevant in the cultivation of citrus. Greenhouse tomatoes use fresh soil to cultivate the crops. Therefore there are also no limitations of succeeding crops.

B.3.2.5 Proposed instructions for use as printed, or to be printed, on labels (based on document E)

Labels have been submitted.

B.3.3 Summary of data on application

See Table 3.3-01.

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

Table 3.3-01 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 - 3.7, 3.9)

Summary of representative uses evaluated (pyridaben)

Crop and / or situation (a)	Member State or Country	Product name	F G or (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Citrus	Southern MS	Nexter Pro, Sanmite 75 WP	F	Mites Whitefly	WP	750 g/l	Tractor mounted / trailed broadcast air assisted sprayer	At infestation on No later than BBCH 83	1	na	0.005 – 0.04	750 - 6000	0.3	14	
Tomato	Northern and Southern MS	Nexter Pro, Sanmite 75 WP	G	Mites Whitefly	WP	750 g/l	Various hydraulic sprayers	At infestation on No later than BBCH 89	1	na	0.005 – 0.04	625 - 5000	0.25	3	

- (a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
- (c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
- (f) All abbreviations used must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

- (i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypry). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthialcalcarb-isopropyl).**
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (k) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)
- (m) PHI - minimum pre-harvest interval

B.3.4 Further information on the active substance (Annex IIA 3.7 to 3.9)**B.3.4.1 Recommended methods and precautions concerning handling, storage, transport or fire (Annex IIA 3.7)****B.3.4.1.1 Handling**

The usual precautions for handling chemicals should be observed. Wear suitable respirator, protective clothing, shoes, gloves and goggle. Do not eat, drink or smoke during the work.

Do not breathe dust. Avoid contact with skin or eyes. Protect containers against physical damage. Keep tightly closed in original labeled container. Keep away from heat and open flame. Prevent spillage from entering the drainage systems or watercourses.

Do not re-use this container for any other purpose. Keep away from possible contact with water. Keep away from reach of children. Keep away from foods, drinks and animal feeding stuffs. Store in a cool place and protect from direct sunlight.

B.3.4.1.2 Storage

See B.3.4.1.1.

B.3.4.1.3 Transport

Those directly responsible for transport must know what their loads contain, and what action must be taken in the event of emergency. Special care must be taken during loading and unloading to prevent damage to containers.

Land transport:

ADR/RID: Class 6.1

Warning sign, Hazard No. 6.1

UN No.: 2588

Packing group: I

Proper shipping name: None

Sea transport:

IMO/IMDG: Class 6.1

UN No: 2588

Packing group: I

EMS: None

Marine pollutant: Marine Pollutant

Proper shipping name: Pesticide, solid, toxic, n.o.s. (Pyridaben)

Air transport:

ICAO/IATA: Class 6.1

Un850.: 2588

Packing group: I

Proper shipping name: Pesticide, solid, toxic, n.o.s. (Pyridaben)

FireExtinguish media: water, foam, dry chemicals or CO₂.

Special fire fighting procedures: use self-contained breathing apparatus and protective clothing. Move away this product from fire if there is no risk. Use water spray of fog nozzle to keep containers or surrounding area cool. Fight fire from upwind position.

Unusual fire and explosion hazards: keep away from heat and open flame.

Hazardous combustion products: combustion can form carbon monoxide, nitrogen oxides, sulfur dioxide and hydrogen chloride.

B.3.4.2 Procedures for destruction or decontamination of the active substance, contaminated packaging and contaminated material**B.3.4.2.1 Controlled incineration**

Pyridaben does not have a halogen content greater than 60%, hence pyrolytic behaviour under controlled conditions is not required. The recommended means of safe disposal is by controlled incineration at an approved chemical waste facility (combustion temperature > 1100°C, presence of more than 6% oxygen, residence time at least 2 seconds). The whole incineration system should include a scrubber and neutralization process for emission.

B.3.4.2.2 Others

Wastes resulting from manufacture and formulation that can not be used or chemically reprocessed, uncleaned empty containers and other contaminated materials should be disposed of in a land fill approved for pesticide disposal or at a suitable incineration plant in accordance with the applicable official regulations.

B.3.4.3 Emergency measures in the case of an accidentContainment of spillages in water:

Personal precautions: Wear suitable respirator protective clothing, shoes, gloves and goggles.

Environmental precautions: Prevent spillage from entering the drainage systems or watercourses.

Methods for cleaning: Keep unauthorised persons, children and animals away from the affected area. Prevent further waste by closing the container properly, shifting its position to stop leakage or placing into another container. Carefully sweep up and collect the spilled material by absorbent such as sand or vermiculite and place in a closed container (drum) for disposal. Do not raise dust. Wash affected area with water containing a strong industrial type detergent.

B.3.4.4 Summary of further information and assessment

No further information.

B.3.5 Further information of the plant protection product (Annex IIIA 4)

Product name: Nexter Pro

B.3.5.1.1 Packaging, compatibility on the preparation with proposed packaging materials (Annex IIIA 4.1)

It is proposed that Nexter Pro is packed in water soluble bags.

0.2 kg bag:

Closure	: not relevant since this bag is completely sealed
Filling quantity	: content 0.2 kg
Material	: Cold water soluble, polyvinyl alcohol (PVA) bag
Dimensions	: 7.5 X 0 X 1.25 cm
Capacity	: 0.2 kg

External packaging:

Corrugated, double wall, fibreboard shipping case to hold five 0.2 kg bags of product. GMA Grade A partial 4-way flush stringer wood pallet.

B.3.5.1.2 Packaging suitability

Individual bags containing Nexter Pro examined during testing were soft, flexible and free from ruptures. There was no evidence of caking of the test substance in the bags and there were no leakage of the material from the bags.

B.3.5.1.3 Packaging resistance

After 2 years of storage of the water soluble bags containing Nexter Pro at ambient temperature, the bags showed no sign of deformation or any signs of damage. Nexter Pro is considered to be stable for 2 years in the commercial package.

B.3.5.2 Procedures for cleaning application equipment (Annex IIIA 4.2)

Wear appropriate protective equipment. The polar surface of the material presents little affinity to the non-polar active ingredient. The container should be washed with water (5% of the container's volume), sprayed out and followed by a further wash with water (5% of the container's wash). Finally the container was filled with an acetonitrile/water mix.

B.3.5.3 Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment (Annex IIIA 4.3)**Pre-harvest interval (in days)**

When the formulation is applied according to the good agricultural practices and to the label recommendations a PHI of 14 and 3 days is proposed for citrus and tomato respectively.

Re-entry period (in days) for livestock, to areas to be grazed.

For citrus the a re-entry period is not relevant since citrus orchards are not to be grazed. A re-entry period is also not relevant for tomato since it concerns a glasshouse application.

Re-entry period (in hours or days) for man to crops, buildings or spaces treated

Nexter Pro is used on citrus orchards and glasshouse tomatoes and it is not necessary to enter the crop shortly after spraying. Therefore it is not necessary to determine a particular re-entry time for workers.

Withholding period (in days) for animal foodstuffs

No withholding period is defined (use on tomatoes and citrus which are normally not fed to livestock).

Waiting period (in days) between application and handling treated products

See re-entry period.

Waiting period (in days) between last application and sowing or planting of succeeding crops

Not relevant for citrus and tomatoes since citrus orchards are permanent cultures and use of pyridaben in tomatoes will not result in significant uptake by succeeding crops.

For spray operatives and workers risk assessments presented in Annex III Section 3 Points 7.2.1 and 7.2.3. indicate no concern. Therefore a waiting period before handling treated products could be proposed as: If necessary – allow treated crop to dry after spraying before handling.

Conditions under which the product should not be used

No restrictions should be imposed on the use of the product in relation to specific agricultural, plant health or environmental conditions. However, pyridaben is more effective if the treatments are carried out with a sufficient amount of water to ensure thorough coverage of foliage and fruit. Favourable growth conditions at the time of and after treatment ensure the efficacy of the product.

B.3.5.4 Recommended methods and precautions concerning: handling, storage, transport or fire (Annex IIIA 4.4)**Handling**

When handling the concentrated product (e.g. decanting or preparing the ready for use product) wear an overall, long rubber apron, gloves, goggles and use a fume hood or adequate ventilation and/or half mask (S40).

Prevent dust formation – may form explosive mixtures in air. Electrostatic charges should be prevented and contact with ignition sources avoided (S49).

Storage

The usual precautions for storage of chemicals should be observed. Store in a dry place below 30°C separate from food, feed and consumable items (S49). Further details in MSDS of Nexter Pro (Sanmite 75 WP).

TransportLand transport:

ADR/RID:	Class 9
UN No.:	3077
Packing group:	III
Proper shipping name:	Environmentally hazardous substance, solid n.o.s. (contains: Pyridaben 75%) (S49)

Sea transport:

IMO/IMDG:	Class 9
UN No:	3077
Packing group:	III
EMS:	None
Marine pollutant:	yes
Proper shipping name:	Environmentally hazardous substance, solid n.o.s. (contains: Pyridaben 75%) (S49)

Air transport:

ICAO/IATA: Class 9
Un No.: 3077
Packing group: III
Proper shipping name: Environmentally hazardous substance, solid n.o.s. (contains: Pyridaben 75%) (S49)

For further details reference is made to the MSDS of Nexter Pro.

FireFire-fighting measures:

Fight fires with suitable extinguishing media (water spray, foam and dry extinguishing media) wearing a self-contained breathing apparatus and chemical protective clothing. Contaminated extinguisher water should not be allowed to reach sewerage or effluent systems. Dispose of fire debris and contaminated extinguisher water in accordance with official regulations. Carbon monoxide, hydrogen chloride, nitrogen oxides and sulfur oxides can be released in case of fire.

For further details reference is made to the MSDS of Nexter Pro.

Waste

It is recommended to purchase and store quantities of product expected to be used in one season. Do not mix a volume of spray-mixture, which is greater than the volume necessary for the area planned to be treated. Dilute residual tank mixes remaining in the spray equipment in the ratio 1:10 and apply it on the treated area.

B.3.5.5 Emergency measures in the case of an accident (Annex IIIA 4.5)Containment of spillages:

Contain with suitable absorbent material and dispose in accordance with local regulations using appropriate personal precautions (including breathing apparatus).

For further details reference is made to the MSDS of Nexter Pro.

Decontamination of areas, vehicles and buildings:

Water and detergents are the recommended cleaning material (S49). Product should be disposed of by special means, e.g. suitable incineration or dumped, in accordance with local regulations. Contaminated packaging that cannot be cleaned should be disposed of as for product (S49).

Use the personal protective equipment as proposed above (S49).

For further details reference is made to the MSDS of Nexter Pro.

First aid:

- General: Remove contaminated clothing and move to fresh air; in case of fainting bring in stable lateral position; apply artificial respiration if not breathing. If difficulties occur: obtain medical attention.
- Show container, label and/or safety sheet to physician (S40 and S49).
- After skin contact: Wash contaminated skin and mucous membranes immediately with plenty of water using soap if available (S40 and S49).
- After eye contact: Wash affected eyes for at least 15 minutes under running water with eyelids open, consult an eye specialist (S49).
- After ingestion: Rinse mouth immediately and then drink plenty of water, induce vomiting, obtain medical attention in all cases (S49). Avoid giving re-absorption stimulating substances like fats or alcohol. Give activated charcoal (medicinal charcoal). Get medical attention (S40).
- Note to physician: treat according to symptoms (decontamination, vital functions), no known specific antidote (S49).

B.3.5.6 Procedures for destruction or decontamination of the plant protection product and its packaging (Annex IIIA 4.6)**B.3.5.6.1 Possibility of neutralisation**

A neutralisation procedure cannot be proposed.

B.3.5.6.2 Controlled incineration

The recommended means of safe disposal is by controlled incineration at an approved chemical waste facility. For further details reference is made to the MSDS of Nexter Pro.

B.3.5.6.3 Others

No other method than controlled incineration for disposal of the plant protection product, contaminated packaging and contaminated materials is available.

B.3.5.7 Summary of further information and assessment

No further information.

B.3.6 References relied on**References for the active substance**

Annex Point IIA	Author(s)	Year	Title Company, Report No GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
IIA, 3.5.1/01	Hollingworth, R. M.; Ahammadsahib, K. I.; Gadelhak, G.; McLaughlin, J. L.	1994	New inhibitors of Complex I of the mitochondrial electron transport chain with activity as pesticides Biochemical Society Transactions Vol 22, pp230-233 (1994) GLP not relevant, Published	N	-
IIA, 3.5.1/02	Schuler, F.; Yano, T.; Di Bernardo, S.; Yagi, T.; Yankovskaya, V.; Singer, T. P.; Casida, J. E.	1999	NADH-quinone oxidoreductase: PSST subunit couples electron transfer from iron sulfur cluster N2 to quinone Proceedings of the National Academy of Science USA Vol 96, pp4149-4153 (March, 1999) GLP not relevant, Published	N	-
IIA, 3.5.1/03	Schuler, F.; Casida, J. E.	2001	The insecticide target in the PSST subunit of complex I Pesticide Management Science Vol 57, pp932-940 (2001) GLP not relevant, Published	N	-
IIA, 3.7	Anonymous	2004	Material Safety Data Sheet (Pyridaben)	Y	NCI

References for the plant protection product

Annex Point IIA	Author(s)	Year	Title Company, Report No GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
IIIA, 4.1.1/01	Anonymous	2003	Packaging component specification – Bag, plastic w / reclosable zipper BASF Agricultural Products Division BASF Aktiengesellschaft Specification no. 67400500 GLP not applicable, Unpublished	Y	BASF
IIIA, 4.1.1/02	Anonymous	2003	Packaging component specification – Film, heat sealable, PVA BASF Agricultural Products Division BASF Aktiengesellschaft Specification no. 2041327 GLP not applicable, Unpublished	Y	BASF
IIIA, 4.1.1/03	Anonymous	2003	Packaging component specification – Carton, corrugated shipping BASF Agricultural Products Division BASF Aktiengesellschaft Specification no. 67400331 GLP not applicable, Unpublished	Y	BASF
IIIA, 4.1.1/04	Anonymous	2002	Packaging component specification – Pallet, wood	Y	BASF

Annex Point IIA	Author(s)	Year	Title Company, Report No GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
			BASF Agricultural Products Division BASF Aktiengesellschaft Specification no. 2040160 GLP not applicable, Unpublished		
IIIA, 4.1.3/01	Sweetapple, G. G.	1992	Pyridaben 300 11 I – Determination of corrosion characteristics Ricerca, Inc. BASF Aktiengesellschaft Report no P5WP75 GLP, Unpublished	Y	BASF
IIIA, 4.1.3/02	Sotack, G. S.	1998	BAS 300 I: Storage stability and corrosion evaluation of a Pyridaben insecticide formulation in commercial-type packages BASF Corporation BASF Aktiengesellschaft Report no. P12-3WP75 GLP, Unpublished	Y	BASF
IIIA, 4.1.3/03	Comb, A. L.	2003	Pyridaben 75 WP (BAS 300 19 I): Storage stability Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. P19WP75 GLP, Unpublished	Y	NCI
IIIA, 4.2	Ohnsorge, U.	2000	TM Nexter Pro Effectiveness of procedures for cleaning application equipment and protective clothing BASF Aktiengesellschaft Report no. P14WP75 Non-GLP, Unpublished	Y	BASF
IIIA, 4.4/01	Anonymous	1993	Precautions when handling BASF experimental crop protection product BAS 300 11 I BASF Aktiengesellschaft Report no. S40 Non-GLP, Unpublished	Y	BASF
IIIA, 4.4/02	Anonymous	2004	Safety Data Sheet (Sanmite 75 WP) BASF Aktiengesellschaft Report no. S49 Non-GLP, Unpublished	Y	BASF
IIIA, 4.5/01	Anonymous	1993	Precautions when handling BASF experimental crop protection product BAS 300 11 I BASF Aktiengesellschaft Report no. S40 Non-GLP, Unpublished	Y	BASF
IIIA, 4.5/02	Anonymous	2004	Safety Data Sheet (Sanmite 75 WP) BASF Aktiengesellschaft Report no. S49 Non-GLP, Unpublished	Y	BASF

Annex Point IIA	Author(s)	Year	Title Company, Report No GLP or GEP status Published or not	Data Protection Claimed Y/N	Owner
IIIA, 4.6.2	Anonymous	2004	Safety Data Sheet (Sanmite 75 WP) BASF Aktiengesellschaft Report no. S49 Non-GLP, Unpublished	Y	BASF

B.4 Proposals for classification and labelling

B.4.1 Proposals for the classification and labelling of the active substance (Annex IIA 10)

Physical and chemical properties

Pyridaben is sensitive to friction and is considered to present a danger of explosion (E, R2).

Human health effects

Justified proposals for classification and labelling of the active substance, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	:	T
Indication of danger	:	Toxic
Risk phrases	:	R23; Toxic by inhalation. R25; Toxic if swallowed.
Safety phrases	:	S22; Do not breathe dust. S37; Wear suitable gloves. S38; In case of insufficient ventilation, wear suitable respiratory equipment. S45; In case of accident or if you feel unwell seek medical advice immediately (show the label where possible).

Justification for the proposal

R23	Based on the results of the acute inhalation toxicity study.
R25	Based on the results of the acute oral toxicity studies.
S22	Recommended for substances which are supplied in the form of an inhalable dust.
S37	Obligatory for toxic substances.
S38	Obligatory for substances labelled with R23.
S45	Obligatory for substances labelled with R23 or R25.

Currently, pyridaben is classified in Annex I to Directive 67/548/EEC with (relating to human health effects): R23 and R25.

Ecotoxicological effects

In acute toxicity tests with technical pyridaben in fish, *Daphnia magna* and algae, the lowest LC/EC50 values were 0.73, 1.0 and >13 µg/L, respectively. Pyridaben has a log Pow value of >3, but the experimentally determined BCF is <100 (B.9.2.3). Pyridaben was however not readily biodegradable (B.8.4.3). It is proposed, that on the basis of its acute toxicity pyridaben should be categorised as “Dangerous for the environment” (N), “Very toxic to aquatic organisms” (R50) and “May cause long-term adverse effects in the aquatic environment” (R53).

It is recommended that the active substance also carries the following ‘S’ safety phrases:

- S60 This material and its container must be disposed of as hazardous waste
 S61 Avoid release to the environment. Refer to special instructions/Safety data sheet

B.4.2 Proposals for the classification and labelling the formulation (Annex IIIA 12.3)**Physical and chemical properties**

No classification and labelling is needed based on the physical and chemical properties of Pyridaben 75WP in WSB.

Human health effects

Justified proposals for classification and labelling of the preparation Nexter Pro, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	:	Xi, T ⁺
Indication of danger	:	Irritant; very toxic
Risk phrases	:	R22; Harmful if swallowed. R26; Very toxic by inhalation. R41; Risk of serious damage to eyes.
Safety phrases	:	S22; Do not breathe dust. S26; In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S36; Wear suitable protective clothing. S37; Wear suitable gloves. S38; In case of sufficient ventilation, wear suitable respiratory equipment. S39; Wear eye/face protection. S45; In case of accident or if you feel unwell seek medical advice immediately (show the label where possible).

Justification for the proposal

- R22 Based on the results of the acute oral toxicity study.
- R26 Based on the results of the acute inhalation toxicity study.
- R41 Based on the results of the eye irritation study.
- S22 Recommended for formulations which are supplied in the form of an inhalable dust.
- S26 Obligatory for formulations labelled with R41.
- S36 Obligatory for very toxic formulations.
- S37 Obligatory for very toxic formulations.
- S38 Obligatory for very toxic formulations.
- S39 Obligatory for formulations labelled with R41.
- S45 Obligatory for very toxic formulations.

Ecotoxicological effects

In acute toxicity tests with the Pyridaben 75 WP formulation in fish, *Daphnia magna* and algae, the lowest LC/EC50 values were 2.9, 1.3 and 46000 µg product/L, respectively. Pyridaben has a log Pow value of >3.0, but the experimentally determined BCF is <100 (B.9.2.3). Pyridaben was however not readily biodegradable (B.8.4.3). It is proposed, that on the basis of its acute toxicity the Pyridaben 75 WP formulation should be categorised as “Dangerous for the environment” (N), “Very toxic to aquatic organisms” (R50) and “May cause long-term adverse effects in the aquatic environment” (R53).

It is recommended that the Pyridaben 75 WP formulation also carries the following ‘S’ safety phrases:

- S60 This material and its container must be disposed of as hazardous waste
- S61 Avoid release to the environment. Refer to special instructions/Safety data sheet

B.4.3 References relied on

The proposed classification and labelling for the active substance is based on the evaluation as presented in section B.2, B.6 and B.9.

B.5 Methods of analysis**B.5.1 Analytical methods for technical active substance (Annex IIA 4.1.1) and plant protection product (Annex IIIA 5.1.1)****B.5.1.1 Technical active substance (IIA 4.1.1)****STUDY 1****Characteristics**

Reference	: Stanfield, K.C., 1991a (IIA 4.1.1/01)	GLP statement	: Yes
Type of study	: Analytical methods for technical active substance	Guideline	: EPA 62-3
Year of execution	: 1991	Acceptability	: Acceptable
Test substance	: Pyridaben Technical, Lot no. 900304, 99.7% a.s.	Method reference	: Not reported

Description of the method

Pyridaben Technical was dissolved in acetonitrile together with internal standard (1-phenyl-1-dodecanone). HPLC-UV analysis (240 nm) was performed with an Alltech 5 µm C8 column (4.6 mm i.d. x 25 cm) using acetonitrile/water (3/1) (v/v) as mobile phase.

Results

See Table B.5.1-01.

Conclusion

The method is acceptable for the determination of pyridaben in technical material.

Remarks

None.

STUDY 2**Characteristics**

Reference	: Anonymous, 1999a (IIA 4.1.1/02)	GLP statement	: No
Type of study	: Analytical methods for technical active substance	Guideline	: CIPAC Pyridaben 583
Year of execution	: Not applicable	Acceptability	: Acceptable
Test substance	: Pyridaben Technical	Method reference	: CIPAC Pyridaben 583

Description of the method

The method was CIPAC method Pyridaben 583 for Pyridaben Technical.

Pyridaben Technical was dissolved in acetonitrile together with internal standard (1-phenyl-1-dodecanone). HPLC-UV analysis (240 nm) was performed with Nucleosil 5 µm C8 column (4.6 mm i.d. x 25 cm) using acetonitrile/water (3/1) (v/v) as mobile phase.

Results and evaluation

See Table B.5.1-01. The method was based on and essentially identical to that of the previous study. Data on the results of calibration were not provided in the description of the method. CIPAC methods however are considered to be sufficiently validated and are acceptable.

Conclusion

The method is acceptable for the determination of pyridaben in technical material.

Remarks

None.

B.5.1.2 Plant protection product (IIIA 5.1.1)

STUDY 1

Characteristics

Reference	: Anonymous, 1999b (IIIA 5.1.1/01)	GLP statement	: Not applicable
Type of study	: Analytical methods for plant protection product	Guideline	: CIPAC method 583
Year of execution	: Not applicable	Acceptability	: Acceptable
Test substance	: Pyridaben wettable powders	Method reference	: CIPAC method 583

Description of the method

The method was CIPAC method Pyridaben 583 to determine pyridaben in pyridaben wettable powders.

Pyridaben wettable powder was dissolved in acetonitrile containing 1-phenyl-1-dodecanone as an internal standard. Pyridaben was analyzed by HPLC (Nucleosil C8, 250 mm x 4.6 mm i.d., 5 µm) using 3/1 (v/v) acetonitrile/water as mobile phase with UV detection at 240 nm.

Results

See Table B.5.1-01. The method was based on and essentially identical to that of study 3. It was stated that HPLC-DAD could be used to confirm compound identity. Data on the results of calibration and on interference (chromatogram) were not provided in the description of the method. CIPAC methods however are considered to be sufficiently validated and are acceptable.

Conclusion

The method is acceptable for the determination of pyridaben in Pyridaben wettable powders.

Remarks

None.

STUDY 2

Characteristics

Reference	: Petersen M. (IIIA 5.1.1/02)	GLP statement	: Yes
Type of study	: Analytical methods for plant protection product	Guideline	: Not stated
Year of execution	: 1991-1992	Acceptability	: Not acceptable
Test substance	: BAS 300 11 I, batch no. AF 137-50, 75.8% a.s.	Method reference	: CP 159

Description of the method

The results were reported of a reversed phase HPLC/UV method to determine BAS 300 11 I in water.

Results and evaluation

See Table B.5.1-01. The data submitted (determination of pyridaben based product in water at 0.25-50 mg/L) do not address the data requirement (determination of pyridaben in pyridaben wettable powder). Furthermore, the report lacked documentation on, amongst other things: sample work-up; analytical method; method to quantify residues. Chromatograms were not reported and data on linearity and precision were not available.

Conclusion

The method is not acceptable for the determination of pyridaben in Pyridaben wettable powders.

Remarks

No further remarks.

STUDY 3**Characteristics**

Reference	: Stanfield, K.C., 1991b (IIIA 5.1.1/03)	GLP statement	: Yes
Type of study	: Analytical methods for plant protection product	Guideline	: EPA 62-3
Year of execution	: 1991	Acceptability	: Acceptable
Test substance	: BAS 300 11 I, pyridaben wettable powder, lot no. AF137-50, 75.8% a.s.	Method references	: Not reported

Description of the method

BAS 300 11 I was dissolved in acetonitrile together with internal standard (1-phenyl-1-dodecanone). HPLC-UV analysis (240 nm) was performed with a Phenomenex 5 µm C8 column (4.6 mm i.d. x 25 cm) using acetonitrile/water (3/1) (v/v) as mobile phase.

Results

See Table B.5.1-01 showing the results for the 75% WP formulation (reported data for a 20% WP formulation are not shown but were also acceptable for the parameters that were investigated for the 75% WP formulation).

Conclusion

The method is acceptable for the determination of pyridaben in 75% w/w pyridaben wettable powders.

Remarks

None.

STUDY 4**Characteristics**

Reference	: Anonymous, 1990 (IIIA 5.1.1/04)	GLP statement	: No
Type of study	: Analytical methods for plant protection product	Guideline	: Not stated
Year of execution	: Not reported	Acceptability	: Not acceptable
Test substance	: Pyridaben 20% wettable powder	Method references	: Not reported

Description of the method

Pyridaben 20% WP was dissolved in acetonitrile together with internal standard (1-phenyl-1-dodecanone). HPLC-UV analysis (240 nm) was performed with a Nucleosil 5 µm C8 column (4.6 mm i.d. x 25 cm) using acetonitrile/water (3/1) (v/v) as mobile phase.

Results and evaluation

See Table B.5.1-01 showing the results for a 20% WP formulation. The parameters investigated (linearity, precision) were acceptable. Interference was not addressed (no chromatogram of blank formulation), and accuracy was not determined. As the report was unsigned, this study is not acceptable. The method however should be acceptable for 75% WP formulations as it was identical to that evaluated in the previous three studies.

Conclusion

The study is not acceptable.

Remarks

No further remarks.

Table B.5.1-01 Summary of method validation (pyridaben in technical active material and formulations).

	Linearity (between)	Precision – Repeatability	Precision – Reproducibility	Accuracy (%)	Interference/Specificity	Ref.
Method Reference: not reported Pyridaben in technical material	0.017 ± 0.083 mg/mL n=5 ($r^2 = 1.0000$)	n=5, triplicate injections, at 1 concentration, (RSD 0.9%)	Not determined.	Not determined.	No interference.	Stanfield K.C., 1991a (4.1.1/01)
Method Reference: CIPAC Pyridaben 583 Pyridaben in technical material	no data	Repeatability $r = 9$ g/kg at 994 g/kg a.s. content	Reproducibility R = 10 g/kg at 994 g/kg a.s. content	Not determined.	No interference.	Anonymous, 1999a (4.1.1/02)
Method Reference: CIPAC Pyridaben 583 Pyridaben in pyridaben wettable powders	no data	Repeatability $r = 9$ g/kg at 752 g/kg a.s. content	Reproducibility R = 11 g/kg at 752 g/kg a.s. content	Not determined.	Not determined.	Anonymous, 1999b (5.1.1/01)
Method Reference: CP 159 BAS 300 11 I (75.8% Pyridaben)	no data	Not determined.	Not determined.	Recovery from water fortified at 0.25, 2.5, 9.9, 25 and 50 mg product/L: 100.6, 99.4, 99.7, 99.3 and 100.5% respectively	no data	Petersen M., 1992 (5.1.1/02)
Method Reference: not reported Pyridaben in pyridaben wettable powders	0.017 – 0.083 mg/mL n=5 ($r^2 = 1.000$)	n=5, triplicate injections, at 1 concentration, (RSD 0.6%)	Not determined.	Recovery from blank BAS 300 11 I spiked at 75% w/w: 99.2% & 100.5% (n=2)	No interference.	Stanfield K.C., 1991b (5.1.1/03)

	Linearity (between)	Precision – Repeatability	Precision – Reproducibility	Accuracy (%)	Interference/Specificity	Ref.
Method Reference: not reported Pyridaben 20% wetable powder	0.017 – 0.083 mg/mL n=5 ($r^2 = 1.0000$)	n=5, triplicate injections, at 1 concentration, (RSD 0.5%)	Not determined.	Not determined.	No interference.	Anonymous, 1990 (5.1.1/04)

B.5.2 Analytical methods (residue) for plants, plant products, foodstuffs of plant and animal origin, feedingstuffs (Annex IIA 4.2.1 and Annex IIIA 5.2)

The following residue definitions were determined (section B.7):

Residue definition for plant products

The residue definition for post-registration monitoring and for risk assessment is proposed as pyridaben for tomato and citrus.

Residue definition for animal products

No definition of residues in animal products was required, as no significant residues are expected in products of animal origin.

STUDY 1

Characteristics

Reference	: Tilting, N., 1991 (IIA 4.2.1/01)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: EPA 71-4
Year of execution	: 1989-1990	Acceptability	: Acceptable for pre-registration for apples, pears, strawberry, tomatoes and peppers.
Test substance	: Pyridaben, 99.6% pure	Method reference	: 938/1

Description of the method

Methods were described to determine pyridaben and its photodimeric metabolite pyridaben D-1 in plant samples. Only data on pyridaben have been summarised.

Pyridaben is extracted from cotton seed with methanol, and from other plant material with 0.1M AgNO₃ in water/acetone followed by water/acetone. After filtration and evaporation of organic solvent the residues are partitioned into dichloromethane or hexane (depending on the plant material, no partitioning performed for cotton seed). The organic phase is cleaned up by GPC (citrus fruit only), followed by a Florisil or activated charcoal/Florisil column cleanup (others). Analysis is by GC/ECD on a SE 54 capillary column (21 m length x 0.28 mm I.D., 0.27 µm film thickness).

Results

See Table B.5.2-01.

Conclusions

- The method is not accepted for post-registration purposes (no confirmatory method).
- The method is acceptable for pre-registration with an LOQ of 0.05 mg/kg for the following samples: apples, pears, strawberry, tomatoes and peppers.
- The LOQ of 0.05 mg/kg for orange fruit (see remark 2 & 3) and grape and peach (see remark 3), and that of 0.01 mg/kg for orange juice and of 0.1 mg/kg for cotton seed (see remark 3 & 4) are not accepted.

Remarks

1. A handwritten comment in the report stated that 0.1M AgNO₃ was only needed for the extraction of the photodimeric metabolite pyridaben D-1, not for pyridaben.
2. An interfering peak occurred in chromatograms of untreated orange at the retention time of pyridaben. The height of this peak represented about 40% (and the area presumably also) of the height (area) of the pyridaben peak at the claimed LOQ (0.05 mg/kg). The LOQ of 0.05 mg/kg is therefore **not acceptable for orange fruit** (lowest validated level is 5.0 mg/kg).
3. Replication was less than recommended by the SANCO guidelines for analytical methods (n=4 instead of n=5). Considering however the good repeatability, this is considered to be acceptable for all plants materials investigated, **except orange fruit and orange juice, peaches and cotton seed**. The low replication level is also **not accepted for grapes**, since at 5.0 mg/kg three recoveries (all 108%) were close to the upper acceptable limit of 110%, but one recovery was 113% and exceeded the upper limit. A fifth recovery would be required to ascertain acceptable overall mean recovery.
4. For orange juice, mean recovery was outside the 70-110% range at 0.01 mg/kg (63%), and two out of four values at 1.0 mg/kg were also <70%. For cotton seed, mean recovery was <70% at both fortification levels. For both samples, the variation (RSD) was high. The method is considered to be **not acceptable for orange juice and cotton seed**.
5. The reports gave some information on a GC/MS method that could be used for confirmation of identity, but provided no validation data. Since this information is not available, the method is not accepted for post-registration purposes.
6. Overall evaluation. The method is **not accepted for post-registration purposes** (no confirmatory method). The method is **acceptable for pre-registration** with an LOQ of 0.05 mg/kg for the following samples: **apples, pears, strawberry, tomatoes and peppers**.

STUDY 2

Characteristics

Reference	: Weidenauer & Ponthet, 1992 (IIA 4.2.1/02)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: -
Year of execution	: 1992	Acceptability	: Not acceptable
Test substance	: Pyridaben, lot no. CH 39/169-1, 99.71% pure	Method reference	: 938/1

Description of the method

An Inter Laboratory Validation (ILV) for method 938/1 (see previous study) was submitted for apples and peaches.

Pyridaben is extracted from apple and peach samples with 0.1M AgNO₃ solution in water/acetone followed by water/acetone. After filtration and evaporation of organic solvent the residues are partitioned into dichloromethane. The organic phase is cleaned up on a Florisil column. Analysis is by GC/ECD on a SPB-5 capillary column (25 m length x 0.32 mm I.D., 0.25 µm film thickness).

Results

See Table B.5.2-01.

Conclusions

The Inter Laboratory Validation for apples and peaches is not acceptable since the submitted data do not support the claimed LOQ of 0.05 mg/kg (see remarks below).

Remarks

1. At the claimed LOQ of 0.05 mg/kg for apples, RSD (24%) was >20%. The submitted data do **not support the claimed LOQ of 0.05 mg/kg for apples**.
2. Replication was less than recommended by the SANCO guidelines for analytical methods (n=4 instead of n=5). At the claimed LOQ of 0.05 mg/kg, RSD for peaches (12%) was high, and two of four recoveries were above upper acceptable limit of 110%. The low replication is not acceptable therefore, and **the submitted data do not support the claimed LOQ of 0.05 mg/kg for peaches**.
3. Overall evaluation. The Inter Laboratory Validation for apples and peaches is not **acceptable** since the submitted data do not support the claimed LOQ of 0.05 mg/kg.

STUDY 3

Characteristics

Reference	: Abdel-Baky <i>et al.</i> , 1994 (IIA 4.2.1/03); amended in 1996	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: EPA 71-4
Year of execution	: 1993	Acceptability	: Acceptable for pre-registration orange peel, orange juice, dried orange pulp & orange molasses. Not acceptable for orange whole fruit and orange oil.
Test substance	: Pyridaben, lot no. CH 39/169-1, 99.7% pure	Method reference	: D9309

Description of the method

Methods were described to determine pyridaben in whole oranges by two different methods, and in processed orange products.

Pyridaben is extracted from homogenised orange and processed orange products with water/acetone, except for dried orange pulp and orange molasses, which are extracted with 0.5N HCl/acetone (1:1) followed by water/acetone, and orange oil, which is extracted with hexane/acetonitrile. The residues are purified by a series of partitions using hexane, acetonitrile, or dichloromethane, depending on the matrix. Further purification is achieved by (mini)column chromatography (Florisil, silica gel and/or C₁₈, depending on the matrix). Analysis is by GC/ECD on a DB-5 capillary column (15 m length x 0.32 mm I.D., 1.0 µm film thickness).

Results

See Table B.5.2-01.

Evaluation

1. The recoveries were corrected for residues in the control samples used for fortification. Residues in control samples of orange peel, orange juice, dried orange pulp and orange molasses were not detectable or insignificant, but residues in control samples of orange whole fruit and orange oil were above 30% of the mean residue at the LOQ (based on peak heights). The LOQ of 0.05 mg/kg is therefore not acceptable for orange whole fruit (lowest validated level is 0.5 mg/kg). The LOQ of orange oil is 0.05 mg/kg. For the other commodities the LOQ is 0.05 mg/kg.
2. The report described a GC/MS method that could be used for confirmation of identity, but provided no validation data except some chromatograms (no recovery and repeatability). Study 10 however provided an ILV including a confirmatory LC-MS/MS method.
3. Note: an ILV confirming the above LOQs for several matrices is provided in study 10 below.

Conclusions

The method is acceptable for pre- and post-registration with an LOQ of 0.5 mg/kg for orange whole fruit and 0.05 mg/kg for orange oil, orange peel, orange juice, dried orange pulp and orange molasses.

Remarks

No further remarks.

STUDY 4

Characteristics

Reference	: Thiem D.A., 1994 (IIA 4.2.1/04)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: EPA 71-4
Year of execution	: 1994	Acceptability	: Acceptable
Test substance	: Pyridaben, lot no. CH 39/169-1, 99.7% pure	Method reference	: D9309

Description of the method

An Inter Laboratory Validation (ILV) for method D9309 (see previous study) was submitted for orange fruit.

Pyridaben is extracted from homogenised orange with water/acetone. The residues are partitioned into hexane, and from hexane into acetonitrile. Further purification is achieved by florisil column chromatography. Analysis is by GC/ECD on a DB-5 capillary column (14.6 m length x 0.32 mm I.D., 1.0 µm film thickness).

Results

See Table B.5.2-01.

Conclusions

The Inter Laboratory Validation was acceptable to support an LOQ of 0.2 mg/kg for whole orange fruit.

Remarks

The Inter Laboratory Validation was acceptable to support an LOQ of 0.2 mg/kg for whole orange fruit.

STUDY 5

Characteristics

Reference	: Abdel-Baky, 1994 (IIA 4.2.1/05)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: EPA 71-4
Year of execution	: 1993	Acceptability	: Acceptable for pre-registration with LOQ 0.05 mg/kg except wet pomace (0.5 mg/kg).
Test substance	: Pyridaben, lot no. 129S8604, 99.5% pure	Method reference	: D9312

Description of the method

Methods were described to determine pyridaben in apples and apple process products.

Pyridaben is extracted from homogenised apple and apple process products with water/acetone. Purification is achieved by mini-column chromatography (C₁₈). Analysis is by GC/ECD on a DB-17 capillary column (30 m length x 0.32 mm I.D., 0.25 µm film thickness).

Results

See Table B.5.2-01.

Conclusions

The method is **not accepted for post-registration purposes** (no confirmatory method). The method is **acceptable for pre-registration** with an **LOQ of 0.05 mg/kg** for all samples **except wet pomace (lowest validated level 0.5 mg/kg)**.

Remarks

1. At the claimed LOQ of 0.05 mg/kg, repeatability was not acceptable for wet pomace (RSD 26%). The LOQ of 0.05 mg/kg is therefore **not acceptable for wet pomace** (lowest validated level is 0.5 mg/kg). For the other commodities the LOQ is 0.05 mg/kg.
2. The reports described a GC/MS method that could be used for confirmation of identity, but provided no validation data. Since this information is not available, the method is not accepted for post-registration purposes.
3. Overall evaluation. The method is **not accepted for post-registration purposes** (no confirmatory method). The method is **acceptable for pre-registration** with an **LOQ of 0.05 mg/kg** for all samples **except wet pomace (lowest validated level 0.5 mg/kg)**.

STUDY 6

Characteristics

Reference	: Perez & Griffin, 1994 (IIA 4.2.1/06)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: EPA 71-4
Year of execution	: 1994	Acceptability	: Acceptable for pre-registration.
Test substance	: Pyridaben, lot no. CH39/169-1, 99.7% pure	Method reference	: D9312

Description of the method

An Inter Laboratory Validation (ILV) for method D9312 (see previous study) was submitted for apples and apple juice.

Pyridaben is extracted from homogenised apple and apple juice with water/acetone. Purification is achieved by mini-column chromatography (C₁₈). Analysis is by GC/ECD on a DB-17 capillary column (30 m length x 0.32 mm I.D., 0.25 µm film thickness).

Results

See Table B.5.2-01.

Conclusion

The Inter Laboratory Validation was acceptable to support an LOQ of 0.4 mg/kg for apple and **apple** juice.

Remarks

Mean recovery at 0.4 mg/kg was >110% for apple juice, but RSD (0.9%) was very low, Therefore the slightly high recovery is acceptable. Replication was limited (n=2), but this is considered to be acceptable for the purpose of an ILV. The Inter Laboratory Validation was acceptable to support an LOQ of 0.4 mg/kg for apple and apple juice.

STUDY 7

Characteristics

Reference	: Abdel-Baky & Malinsky, 1995 (IIA 4.2.1/07)	GLP statement	: Yes
Type of study	: Analytical methods for animal products	Guidelines	: EPA 71-4 (D)
Year of execution	: 1994-1995	Acceptability	: Not acceptable
Test substance	: Pyridaben, lot no. CH39/169-1, purity not reported; Pyridaben-carboxylic acid (PB-7), lot no. PB7-S920822, purity not reported; Pyridaben-alcohol (PB-9), lot no. PB9-S920910, purity not reported.	Method reference	: D9405

Description of the method

Methods were described to determine pyridaben and its metabolites PB-7 (pyridaben-carboxylic acid) and PB-9 (pyridaben-alcohol) in cow's milk and in animal tissues (liver, kidney, muscle and fat).

Pyridaben is extracted from homogenised animal tissue with water/acetone (4:1, v/v) and from milk with acetone. After filtration, an aliquot is methylated by diazomethane, mixed with water and cleaned up using a mini-column (C₁₈). After evaporation and reconstitution in acetonitrile, analysis is by GC/ECD on a DB-17 capillary column (30 m length x 0.32 mm I.D., 0.25 µm film thickness).

Results

See Table B.5.2-01.

Evaluation and conclusion

The validation was sufficient to support and LOQ of 0.01 mg/kg for milk and 0.05 mg/kg for fat, muscle, liver and kidney, for all three analytes, except that insufficient information on a confirmatory method was provided (see Remark 1 below). As the method however used the very toxic diazomethane as methylating agent, **its use for post-registration purposes is not acceptable.** Note: methylation is only needed for GC determination of PB-7 (pyridaben carboxylic acid), not for that of pyridaben and PB-9. The method excluding the methylation step is acceptable for pyridaben and PB-9.

Remarks

1. The reports described a GC/MS method that could be used for confirmation of identity, but provided no validation data except a chromatogram of a standard mixture.
2. The mean recovery of PB-9 from muscle at 0.05 mg/kg (115%) exceeded the upper acceptable limit of 110%, but since the method was very precise (CV 2.6%), this is accepted.

STUDY 8

Characteristics

Reference	: Davis K.V., 1995 (IIA 4.2.1/08)	GLP statement	: Yes
Type of study	: Analytical methods for animal products	Guidelines	: EPA 71-4
Year of execution	: 1994-1995	Acceptability	: Not acceptable
Test substance	: Pyridaben, lot no. CH39/169-1, 99.7% pure; Pyridaben-carboxylic acid (PB-7), lot no. PB7-S920822, 98.8% pure; Pyridaben-alcohol (PB-9), lot no. PB9-S920910, 99.7% pure.	Method reference	: D9405

Description of the method

An Inter Laboratory Validation (ILV) for method D9405 (see previous study) was submitted for liver.

Pyridaben is extracted from homogenised animal tissue with water/acetone (4:1, v/v). After filtration, an aliquot is methylated by diazomethane, mixed with water and cleaned up using a mini-column (C₁₈). After evaporation and reconstitution in acetonitrile, analysis is by GC/ECD on a DB-17 capillary column (30 m length x 0.32 mm I.D., 0.25 µm film thickness).

The following modification to the original method was made, in consultation with the original laboratory:

Because of an enhanced response of PB-9, just prior to GC quantification PEG-400 (0.02%) was added to all samples and standards to prevent enhancement of PB-9. Since PEG-400 produced an interfering peak eluting close to pyridaben, the GC parameters (temperature ramp and column pressure) were modified to give a better separation of pyridaben from the interfering peak.

Results

See Table B.5.2-01. The results shown are for the final analytical run of the study, where PEG-400 (0.02%) was added to all samples and standards.

Conclusion

The Inter Laboratory Validation was acceptable to support an LOQ of 0.05 mg/kg for liver. As the method however used the very toxic diazomethane as methylating agent, **its use for post-registration purposes is not acceptable**. Note: methylation is only needed for GC determination of PB-7 (pyridaben carboxylic acid), not for that of pyridaben and PB-9. The method excluding the methylation step is acceptable for pyridaben and PB-9.

Remarks

None.

STUDY 9

Characteristics

Reference	: Tate S., 2001 (IIA 4.2.1/09)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: SANCO/3029/99
Year of execution	: 2000-2001	Acceptability	: Acceptable for pre-registration with LOQ 0.05 mg/kg; acceptable as ILV for method D9312
Test substance	: Pyridaben, lot no. 129S8604, 100.0% pure	Method reference	: D9312

Description of the method

Methods were described to determine pyridaben in whole tomato.

Pyridaben is extracted from homogenised whole tomato with water/acetone (4:1). After filtration, purification is achieved by mini-column chromatography (C₁₈). Analysis is by GC/ECD on a HP-1 capillary column (30 m length x 0.25 mm I.D., 1 µm film thickness).

Results

See Table B.5.2-01.

Conclusions

The method is **accepted for pre- and post-registration purposes** with an **LOQ of 0.05 mg/kg**. The **method can serve as an ILV for the determination of pyridaben in tomatoes based on the method described in study 5**.

Remarks

The notifier claimed in Tier II of Annex II under point 4, that **the method could serve as an ILV for the determination of pyridaben in tomatoes based on the method described in study 5**, which was validated in an acidic matrix (apples). Evaluation by RMS:

According to SANCO/825/00 rev.6 of 20/06/00 apple is an acidic matrix, but according to RIVM Report 613340006/2003 (RIVM = Rijksinstituut voor Volksgezondheid en Milieu, 2003) apple should be considered a watery matrix. Pyridaben is a neutral analyte, and the extraction solvent in study 5 and 9 is neutral. The validation provided in study 5 for apple should be relevant for tomato, which is a watery matrix. The above method differed from that in study 5 however on the following aspects: the column used was HP-1 capillary column (30 m length x 0.25 mm I.D., 1 µm film thickness) instead of a DB-17 capillary column (30 m length x 0.32 mm I.D., 0.25 µm film thickness); the temperature program of the gas chromatograph was different. Both columns have a slightly different stationary phase (non-polar, 100% dimethylpolysiloxane, for HP-1; medium-polar, (50%-phenyl)-methylpolysiloxane, for DB-17). By adaptation of the temperature program, the retention time of pyridaben was in both cases about 10 minutes, with no interferences present in the proximity of the pyridaben peak. The notifier's claim is **accepted**.

STUDY 10

Characteristics

Reference	: Tate S., 2003 (IIA 4.2.1/10)	GLP statement	: Yes
Type of study	: Analytical methods for plants	Guidelines	: SANCO/3029/99 rev. 4 & SANCO/825/00 rev.6 of 20/06/2000
Year of execution	: 2002-2003	Acceptability	: Acceptable
Test substance	: Pyridaben, lot no. 129S9006, 100.0% pure	Method reference	: Not stated (but comparable to D9309)

Description of the method

Methods were described to determine pyridaben in whole oranges and in processed orange products.

Pyridaben is extracted from homogenised orange and processed orange products with water/acetone, except for orange dry pomace, which is extracted with 0.5N HCl/acetone (1:1) followed by water/acetone. The residues are purified by a series of partitions using hexane, acetonitrile, or dichloromethane, depending on the matrix. Further purification is achieved by mini-column chromatography (Florisil, silica gel and/or C₁₈, depending on the matrix). Analysis is by GC/ECD on a HP-5 capillary column (30 m length x 0.25 mm I.D., 1 µm film thickness).

For confirmation, aliquots of final sample extracts (fortification level 0.5 mg/kg), that were already analysed by GC/ECD, were evaporated, reconstituted in methanol/water and analysed by LC-MS/MS (positive electrospray mode, m/z 365.2>147.1, Phenomenex Luna C8 column, mobile phase water/acetonitrile (1:4)).

Results

See Table B.5.2-01.

Evaluation

The notifier claimed in Tier II of Annex II under point 4, that the method could serve as an ILV for the determination of pyridaben in orange and orange processed products described in study 3. Evaluation by the RMS will consider this claim:

1. The present study 10 was conducted at another laboratory than study 3, as required for an ILV.
2. For whole orange fruit, the LOQ from study 3 was 0.5 mg/kg, since apparent residues in untreated control samples were >30% of the claimed LOQ of 0.05 mg/kg. An ILV for orange fruit from study 4 demonstrated that the LOQ could be set at 0.2 mg/kg. In the present study, apparent residues in untreated control samples were <30% of the claimed LOQ of 0.05 mg/kg. Replication at the claimed LOQ of 0.05 mg/kg (n=3) and at 0.5 mg/kg (n=2) was less than recommended by SANCO/825/00 rev. 6 (n=5). The present study also provided a confirmatory method at 0.5 mg/kg. It is concluded therefore, that the combined information from study 3, 4 and 10 demonstrate that method D9309 is sufficiently validated to support an LOQ of 0.05 mg/kg for whole orange for pre-and post-registration purposes, whereby the present study serves as an ILV for study 3. An LOQ of 0.05 mg/kg is acceptable because it was demonstrated by additional control data that apparent residues in a range of untreated orange samples, obtained from various sources, are <30% of the claimed LOQ of 0.05 mg/kg.
3. In the present study, replication at the claimed LOQ of 0.05 mg/kg and higher levels (n=2 or n=3) was less than recommended by SANCO/825/00 rev. 6 (n=5) for orange peel, dried orange pulp and orange juice, for which the LOQ from study 3 was 0.05 mg/kg. The present study also provided a confirmatory method, which was missing in study 3. It is concluded therefore, that the combined information from

study 3 and study 10 demonstrate that method D9309 is sufficiently validated to support an LOQ of 0.05 mg/kg for orange peel, dried orange pulp and orange juice for pre-and post-registration purposes, whereby the present study serves as an ILV for study 3.

4. In the present study, replication at the claimed LOQ of 0.05 mg/kg and higher levels (n=2 or n=3) was less than recommended by SANCO/825/00 rev. 6 (n=5) for orange pulp. Since orange pulp is an easier matrix than whole orange, and the methods for whole orange and orange pulp were identical, the validation for whole orange and orange pulp may be combined for evaluation of the LOQ of orange pulp. The combined data for whole orange and orange pulp from the present study support an LOQ of 0.05 mg/kg (including a confirmatory method). Based on the fact that in study 3 the LOQ for dried orange pulp (a more difficult matrix) was also set to be 0.05 mg/kg, the overall data from two laboratories demonstrate that method D9309 is sufficiently validated to support an LOQ of 0.05 mg/kg for orange pulp.
5. The data from the present study support an LOQ of 0.05 mg/kg for marmalade and canned orange (including a confirmatory method). An ILV is not required since this has been performed already for sufficient other orange matrices.

Conclusions

The method D 9309 is **accepted for pre- and post-registration purposes** with an LOQ of 0.05 mg/kg for whole **orange fruit and orange peel, orange juice, dried orange pulp, orange pulp, orange marmalade and canned orange.**

Remarks

The only difference between the methods in study 3 and 10 was the GC column: study 10 used a HP-5 capillary column instead of a DB-5 capillary column. Both columns however have the same stationary phase material (5%-phenyl)-methylpolysiloxane) and are assumed to give comparable chromatographic separation.

STUDY 11

Characteristics

Reference	: Analytical methods for pesticide residues in foodstuffs (IIA 4.2.1/11)	GLP statement	: -
Type of study	: Analytical methods for plants	Guidelines	: -
Year of execution	: 6e edition, June 1996	Acceptability	: -
Test substance	: -	Method reference	: MRM-1, part -1

Description of the method

The Dutch multi residue method MRM-1, part 1, is proposed as multi residue method. This method is described in the reference stated. The extraction procedure is somewhat similar as the DFG-S19 method, although acetone is the main solvent used instead of acetonitrile. For Pyridaben, no clean-up is proposed and the GC-ITD (gas chromatography with ion trap mass selective detector) is used for detection (3 mass fragments).

Also notifier is indicating that the DFG-S19 method is used by number of commercial companies for pyridaben analysis (no further information given). No validation data on the DFG-S19 method is available.

Results

The method is validated for some matrices, but these are not clearly stated:

<i>Matrices</i>	<i>Spike level</i>	<i>N</i>	<i>Mean Recovery</i>	<i>RSD</i>
Various (non-fatty)	0.29 mg/kg	10	99 %	2.7 %

Only the parent is validated, no other part from the current residue definition.

Conclusions

Although the MRM-1 method is applicable for pyridaben, there is no information on the types of plant matrices for which the method is validated.

Table B.5.2-01 Summary of method description and validation (treated plants, plant products, foodstuffs, feedingsuffs, environmental samples).

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Apples	Pyridaben	0.1M AgNO ₃ in water/ acetone, water/acetone	Dichloromethane partitioning, Florasil column cleanup	GC-ECD	0.05	0.05 5.0	72-80 (76) 73-88 (84)	4.9 (4) 8.9 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Grapes	Pyridaben	As above	As above	GC-ECD	0.05 ^(B)	0.05 5.0	70-73 (72) 108-113 (109)	1.8 (4) 2.0 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Pears	Pyridaben	As above	As above	GC-ECD	0.05	0.05 5.0	79-94 (88) 73-91 (82)	8.0 (4) 9.2 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Peaches	Pyridaben	As above	As above	GC-ECD	0.05 ^(B)	0.05 5.0	88-90 (89) 62-87 (80)	1.2 (4) 15 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Orange (fruit)	Pyridaben	As above	Hexane partitioning, GPC Cleanup, Florasil column cleanup	GC-ECD	0.05 ^(B)	0.05 ^(A) 5.0	86-93 (90) 70-94 (86)	3.6 (4) 12 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Orange (juice)	Pyridaben	As above	As above	GC-ECD	0.01 ^(B)	0.01 1.0	58-68 (63) 61-91 (71)	13 (4) 19.5 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Strawberry	Pyridaben	As above	Hexane partitioning, Activated charcoal/Florasil column cleanup	GC-ECD	0.05	0.05 5.0	84-92 (88) 92-96 (94)	3.5 (4) 1.4 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Tomatoes	Pyridaben	As above	As above	GC-ECD	0.05	0.05 5.0	99-109 (104) 91-98 (95)	4.0 (4) 3.3 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Pepper	Pyridaben	As above	Hexane partitioning, Florasil column cleanup	GC-ECD	0.05	0.05 5.0	72-89 (78) 87-98 (93)	9.3 (4) 4.8 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Cotton seed	Pyridaben	Methanol	Activated charcoal/Florasil column cleanup	GC-ECD	0.1 ^(B)	0.1 5.0	44-77 (65) 58-65 (60)	23 (4) 4.9 (4)	Yes	Tilting N., 1991 (4.2.1/01)
Apples	Pyridaben	0.1M AgNO ₃ in water/ acetone, water/acetone	Dichloromethane partitioning, Florasil column cleanup	GC-ECD	0.05 ^(B)	0.05 5.0	66-108 (89) 87-106 (97)	24 (4) 10 (4)	Yes	Weidenauer & Pontheil, 1992 (4.2.1/02)
Peaches	Pyridaben	As above	As above	GC-ECD	0.05 ^(B)	0.05 5.0	88-114 (105) 92-101 (96)	12 (4) 4.3 (4)	Yes	Weidenauer & Pontheil, 1992 (4.2.1/02)

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Orange (whole fruit)	Pyridaben	water/ acetone	Hexane partitioning, hexane/acetone/nitrile partitioning, Florisil column cleanup	GC-ECD	0.05 ^(B)	0.05 0.5 5.0	77-93 (86) 76-92 (87) 78-96 (90) ^(C)	8.4 (6) 6.8 (6) 7.9 (6)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Orange (whole fruit) <u>alternative procedure</u>	Pyridaben	As above	Dichloromethane partitioning, silica gel column cleanup	GC-ECD	0.05 ^(B)	0.05 0.5 5.0	77-93 (84) 77-93 (84) 79-94 (85) ^(C)	5.8 (9) 6.1 (9) 5.4 (9)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Orange peel	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, silica gel column cleanup, C18 column cleanup	GC-ECD	0.05	0.05 0.5 5.0	87-120 (97) 85-93 (90) 71-97 (88)	12 (6) 3.4 (6) 10 (6)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Orange juice	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, Florisil column cleanup	GC-ECD	0.05	0.05 0.5 5.0	87-98 (94) 90-101 (96) 90-100 (94)	4.9 (6) 4.6 (6) 3.9 (6)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Dried orange pulp	Pyridaben	0.5N HCl/acetone (1/1), acetone/water	Hexane partitioning, hexane/acetone/nitrile partitioning, silica gel column cleanup, C18 column cleanup	GC-ECD	0.05	0.05 0.5 5.0	82-92 (86) 80-94 (86) 66-94 (84)	4.7 (6) 6.4 (6) 13 (6)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Orange molasses	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, dichloromethane partitioning, silica gel column cleanup	GC-ECD	0.05	0.05 0.5 5.0	68-109 (88) 56-102 (83) 49-88 (73)	15 (9) 19 (9) 19 (9)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)
Orange oil	Pyridaben	Hexane/ acetone/nitrile (2/1)	Evaporation acetone/nitrile, florisil column cleanup, C18 column cleanup	GC-ECD	0.05	0.05 0.5 5.0	74-85 (81) 76-93 (85) 69-89 (83) ^(C)	5.8 (6) 9.1 (6) 9.0 (6)	Yes	Abdel-Baky <i>et al.</i> , 1994 (4.2.1/03)

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Orange (whole fruit) (ILV)	Pyridaben	water/ acetone	Hexane partitioning, hexane/acetone/nitrile partitioning, Florisil column cleanup	GC-ECD	0.2	0.2 1.0	89-91 (90) 76-87 (82)	2.1 (2) 9.3 (2)	Yes	Thiem D.A., 1994 (4.2.1/04)
Apple (whole fruit)	Pyridaben	As above	C18 mini-column cleanup	GC-ECD	0.05	0.05 0.5 5.0	75-96 (88) 88-98 (92) 85-92 (90)	10 (5) 4.0 (6) 3.2 (6)	Yes	Abdel-Baky, 1994 (4.2.1/05)
Apple (wet pomace)	Pyridaben	As above	As above	GC-ECD	0.05 ^(B)	0.05 0.5 5.0	68-132 (90) 93-101 (98) 94-106 (100)	26 (6) 3.1 (6) 4.6 (6)	Yes	Abdel-Baky, 1994 (4.2.1/05)
Apple (dry pomace)	Pyridaben	As above	As above	GC-ECD	0.05	0.05 0.5 5.0	77-105 (89) 76-98 (89) 70-102 (94)	11 (6) 8.9 (6) 13 (6)	Yes	Abdel-Baky, 1994 (4.2.1/05)
Apple juice	Pyridaben	As above	As above	GC-ECD	0.05	0.05 0.5 5.0	96-110 (105) 63-101 (88) 82-99 (93)	4.6 (6) 16 (6) 6.7 (6)	Yes	Abdel-Baky, 1994 (4.2.1/05)
Apple (whole fruit) (ILV)	Pyridaben	As above	As above	GC-ECD	0.4	0.4 2.0	98-120 (109) 98-99 (98)	15 (2) 1.2 (2)	Yes	Perez & Griffin, 1994 (4.2.1/06)
Apple juice (ILV)	Pyridaben	As above	As above	GC-ECD	0.4	0.4 2.0	113-114 (114) 98-99 (98)	0.9 (2) 1.1 (2)	Yes	Perez & Griffin, 1994 (4.2.1/06)
Milk	Pyridaben	acetone	Filtration, methylation with diazomethane, C18 mini-column cleanup	GC-ECD	0.01	0.01 1.0	68-85 (77) 93-101 (97)	10 (5) 3.2 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Kidney	Pyridaben	water/ acetone	As above	GC-ECD	0.05	0.05 1.0	78-107 (91) 96-106 (101)	15 (6) 3.6 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Muscle	Pyridaben	As above	As above	GC-ECD	0.05	0.05 1.0	95-105 (99) 85-94 (91)	3.4 (6) 4.2 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Fat	Pyridaben	As above	As above	GC-ECD	0.05	0.05 1.0	70-92 (81) 86-88 (87)	12 (6) 0.7 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Liver	Pyridaben	As above	As above	GC-ECD	0.05	0.05 1.0	89-110 (94) 96-105 (102)	8.5 (6) 3.1 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Milk	PB-7 (pyridaben- carboxylic acid)	acetone	As above	GC-ECD	0.01	0.01 1.0	66-85 (76) 88-100 (94)	8.6 (5) 4.9 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Kidney	PB-7 (pyridaben- carboxylic acid)	water/ acetone	As above	GC-ECD	0.05	0.05 1.0	67-83 (77) 73-85 (78)	8.0 (6) 6.3 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Muscle	PB-7 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	80-95 (89) 61-85 (75)	6.0 (6) 13 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Fat	PB-7 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	85-103 (94) 92-97 (96)	8.6 (6) 1.9 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Liver	PB-7 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	79-100 (91) 88-103 (96)	8.4 (6) 6.5 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Milk	PB-9 (pyridaben- alcohol)	acetone	As above	GC-ECD	0.01	0.01 1.0	88-101 (97) 96-111 (103)	5.6 (5) 5.3 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Kidney	PB-9 (pyridaben- carboxylic acid)	water/ acetone	As above	GC-ECD	0.05	0.05 1.0	87-123 (106) 99-115 (110)	14 (6) 5.6 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Muscle	PB-9 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	111-119 (115) 82-96 (91)	2.6 (6) 6.3 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Fat	PB-9 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	86-118 (105) 87-99 (93)	12 (6) 5.0 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Liver	PB-9 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 1.0	92-117 (100) 97-116 (105)	9.6 (6) 7.8 (6)	Yes	Abdel-Baky & Malinsky, 1995 (4.2.1/07)
Liver	Pyridaben	As above	As above	GC-ECD	0.05	0.05 0.25	94-99 (96) 89-90 (90)	3.7 (2) 1.3 (2)	Yes	Davis K.V., 1995 (4.2.1/08)
Liver	PB-7 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 0.25	78-83 (80) 78-91 (84)	4.0 (2) 11 (2)	Yes	Davis K.V., 1995 (4.2.1/08)
Liver	PB-9 (pyridaben- carboxylic acid)	As above	As above	GC-ECD	0.05	0.05 0.25	78-81 (80) 75-94 (84)	2.4 (2) 16 (2)	Yes	Davis K.V., 1995 (4.2.1/08)
Tomato	Pyridaben	As above	C18 mini-column cleanup	GC-ECD	0.05	0.05 0.5 5.0	70-94 (85) 86-91 (89) 84-100 (92)	11 (5) 2.6 (5) 6.5 (5)	Yes	Tate S., 2001 (4.2.1/09)
Orange (whole fruit)	Pyridaben	As above	Dichloromethane partitioning, silica gel column cleanup	GC-ECD	0.05	0.05 0.5 1.0	94-110 (103) 92-104 (98) 87-97 (92)	7.9 (3) 8.7 (2) 5.5 (3)	Yes	Tate S., 2003 (4.2.1/10)
Orange pulp	Pyridaben	As above	As above	GC-ECD	0.05	0.05 0.5 1.0	97-108 (104) 108-110 (109) 86-93 (90)	5.7 (3) 1.3 (2) 3.9 (3)	Yes	Tate S., 2003 (4.2.1/10)
Orange peel	Pyridaben	As above	Hexane partitioning, hexane/acetonitrile partitioning, silica gel & C18 column cleanup	GC-ECD	0.05	0.05 0.5 1.0	84-90 (87) 108-108 (108) 75-100 (84)	3.5 (3) 0.0 (2) 17 (3)	Yes	Tate S., 2003 (4.2.1/10)
Marmalade	Pyridaben	As above	As above	GC-ECD	0.05	0.05 0.5 1.0	83-99 (92) 110-110 (110) 79-94 (89)	6.4 (5) 0.0 (2) 6.8 (5)	Yes	Tate S., 2003 (4.2.1/10)

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Orange dry pomace	Pyridaben	0.5N HCl/acetone (1/1) & acetone/water	As above	GC-ECD	0.05	0.05 0.5 1.0	73-76 (74) 76-82 (79) 70-84 (78)	2.1 (3) 5.4 (2) 9.2 (3)	Yes	Tate S., 2003 (4.2.1/10)
Canned orange	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, silica gel column cleanup	GC-ECD	0.05	0.05 0.5 1.0	102-108 (105) 110-110 (110) 102-109 (106)	2.5 (5) 0.0 (2) 3.0 (5)	Yes	Tate S., 2003 (4.2.1/10)
Orange juice	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, Florisil column cleanup	GC-ECD	0.05	0.05 0.5 1.0	86-91 (88) 102-102 (102) 76-78 (77)	2.8 (3) 0.0 (2) 1.5 (3)	Yes	Tate S., 2003 (4.2.1/10)
Orange (whole fruit)	Pyridaben	water/ acetone	Dichloromethane partitioning, silica gel column cleanup	LC-MS/MS	-	0.5	74-84 (79)	9.0 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Orange pulp	Pyridaben	As above	As above	LC-MS/MS	-	0.5	70-76 (73)	5.8 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Orange peel	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, silica gel & C18 column cleanup	LC-MS/MS	-	0.5	94-94 (94)	0.0 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Marmalade	Pyridaben	As above	As above	LC-MS/MS	-	0.5	84-88 (86)	3.3 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Orange dry pomace	Pyridaben	0.5N HCl/acetone (1/1) & acetone/water	As above	LC-MS/MS	-	0.5	72-74 (73)	1.9 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Canned orange	Pyridaben	water/ acetone	Hexane partitioning, hexane/acetone/nitrile partitioning, silica gel column cleanup	LC-MS/MS	-	0.5	74-86 (80)	1.1 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)
Orange juice	Pyridaben	As above	Hexane partitioning, hexane/acetone/nitrile partitioning, Florisil column cleanup	LC-MS/MS	-	0.5	76-80 (78)	3.6 (2)	No ^(b)	Tate S., 2003 (4.2.1/10)

- (A) An interfering peak occurred in chromatograms of untreated orange at the retention time of pyridaben. The height of this peak represented about 40% (and the area presumably >40%) of the height (area) of the pyridaben peak at the claimed LOQ (0.05 mg/kg).
- (B) Claimed in report, not supported by validation data (see remarks).
- (C) Recoveries were corrected for residue in control samples. The residues in control samples were higher than 30% of the claimed LOQ (see remarks).
- (D) Single point calibration.

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B.5.3 Analytical methods (residue) soil, water, air (Annex IIA 4.2.2 to 4.2.4; Annex IIIA 5.2)

The following residue definition in the environmental compartments soil, water and air was determined in section B.8:

"Detailed guidance to define the environmental residue is not available. Provisionally therefore, the active substance and major metabolites are listed in the definition. No metabolites were formed at >10% AR under aerobic laboratory conditions in soil treated with pyridaben, but PB-4 and PB-7 exceeded 5% AR at 2 consecutive time points (and are hence relevant for exposure of groundwater). The metabolite PB-22 was found at levels up to 13% AR in irradiated soil samples but not in dark controls, and is hence relevant for exposure of soil. PB-7 reached maximum levels in water and sediment of 17% AR and 14% AR respectively. Major aqueous photodegradates of pyridaben were W-1 (max. 27.9% AR, DT50 <1.5 hours, therefore not included in residue definition for air) and B-3 (max. 29.2% AR, photolytically stable)."

The components of the environmental residue are therefore as follows:

Soil: pyridaben, PB-22
 Surface Water: pyridaben, PB-7, W-1, B-3
 Sediment: pyridaben, PB-7
 Ground water: pyridaben, PB-4, PB-7, PB-22
 Air: pyridaben, PB-22, PB-7, B-3"

STUDY 1

Characteristics

Reference	: Tate, S., 2002a (IIA 4.2.2/01)	GLP statement	: Yes
Type of study	: Analytical methods for soil	Guidelines	: SANCO/3029/99 rev. 4.
Year of execution	: 2001	Acceptability	: Acceptable for pyridaben (pre-and post-registration) and P-14 and P-16 (pre-registration)
Test substance	: Pyridaben, batch no. 129S9006, 100.0% pure; soil metabolite P-14, batch no. P-14-S921009, 89.5% pure; soil metabolite P-16, batch no. P-16-S930819, 89.8% pure	Method reference	: Not stated

Description of the method

Methods were described to determine pyridaben and the soil metabolites P-14 (2-*tert*-butyl-4-chloropyradizin-3(2*H*)-one-5-sulfonic acid) and P-16 (4-chloropyradizin)-3(2*H*)-one-5-sulfonic acid) in soil.

Pyridaben and the metabolites P-14 and P-16 are extracted from soil with water/acetone (1:4) followed by methanol/1N phosphoric acid (4:1). An aliquot of the combined extract is centrifuged and filtered (0.45 µm) prior to LC-MS analysis for P-14 (m/z 265) and P-16 (m/z 209) on a Phenomenex SAX column using matrix standards. Another aliquot of the initial extract is cleaned up on a C18 mini column followed by ENVI-Carb

SPE clean-up, and analysed for pyridaben by LC-MS/MS (positive electrospray mode, m/z 365.2>147.1) on a Phenomonex Luna C8 column.

Results

See Table B.5.3-01, which provides validation data for four soils.

Evaluation

The validation was sufficient to support and LOQ in soil of 0.01 mg/kg for all three analytes. The method for P-14 and P-16 (LC-MS) is not sufficiently specific to be used for post-registration. The method for Pyridaben (tandem LC-MS/MS) is sufficiently specific.

Conclusion

The method is suitable for the determination of pyridaben (pre-and post-registration) and P-14 and P-16 (pre-registration) in soil with an LOQ of 0.01 mg/kg.

Remarks

No further remarks.

STUDY 2

Characteristics

Reference	: Delgado N., 1993 (IIA 4.2.3/01)	GLP statement	: Yes
Type of study	: Analytical methods for sediment	Guidelines	: EPA 72-7(a)
Year of execution	: 1992	Acceptability	: Not acceptable (supplementary information)
Test substance	: Pyridaben, batch no. 129S8604, purity not stated	Method reference	: D9201

Description of the method

Methods were described to determine pyridaben in sediment.

Pyridaben is extracted from sediment with methanol, and following evaporation of the methanol cleaned up by dichloromethane partition followed by a Florisil column cleanup. Analysis is by GC/ECD on a DB-5 capillary column (30 m length x 0.32 mm I.D., 1 µm film thickness).

Results

See Table B.5.3-01.

Evaluation

The validation agreed with the requirements for replication laid down in SANCO/3029/99 rev. 4 of 11/07/00 (pre-registration), except for the replication level for determination of accuracy and precision, which was n=4, but should be n=5. Based on the low replication level (n=4), the method fulfilled the other requirements (accuracy, precision, linearity) laid down in SANCO/3029/99 rev. 4 of 11/07/00. Since however the variation at the claimed LOQ of 0.01 mg/kg was high (CV 18%), the low replication is considered an essential guideline deviation. When applying the guideline criteria, the validation is therefore insufficient to support an

LOQ in sediment of 0.01 mg/kg, but it does support an LOQ of 0.5 mg/kg. The results may be used as supplementary information. For pre-registration purposes a LOQ of 0.01 mg/kg can be accepted.

Conclusion

Based on a low replication level (n=4), the method is suitable for the determination of pyridaben in sediment with an LOQ of 0.01 mg/kg. The results may be used as supplementary information.

Remarks

No characteristics (pH, % OC, texture) for the untreated pond sediment used for the fortification experiments were reported.

STUDY 3

Characteristics

Reference	: Tate S., 2002b (IIA 4.2.3/02)	GLP statement	: Yes
Type of study	: Analytical methods for water	Guidelines	: SANCO/3029/99 rev. 4 & SANCO/825/00 rev.6 of 20/06/2000
Year of execution	: 2002	Acceptability	: Acceptable
Test substance	: Pyridaben, batch no. 129S9006, 100.0% pure	Method reference	: Not stated

Description of the method

Methods were described to determine pyridaben in tap, ground and surface (pond) water.

Pyridaben is extracted from water with dichloromethane. After evaporation of the solvent, the extract is cleaned up by SPE on a C18 mini column. Analysis is by LC-MS/MS (positive electrospray mode, m/z 365.2>147.1) on a Phenomenex Luna C8 column, mobile phase 0.01M ammonium acetate/acetonitrile (1:4).

Results

See Table B.5.3-01.

Evaluation and conclusion

The validation is sufficient to support an LOQ of 0.005 µg/L in tap, ground and surface water.

Remarks

No characteristics (pH, TOC) for the untreated pond water used for the fortification experiments were reported.

STUDY 4

Characteristics

Reference	: Betteley J., 2001 (IIA 4.2.4/01)	GLP statement	: Yes
Type of study	: Analytical methods for air	Guidelines	: Incl. SANCO/825/00 rev.6 of 20/06/2000
Year of execution	: 2001	Acceptability	: Acceptable
Test substance	: Pyridaben, lot no. 129S9006, purity 100.0%	Method reference	: Not indicated

Description of the method

The front sections of Tenax adsorption tubes were fortified with 0.36, 1.08 or 10.8 µg pyridaben and air (35°C, 80% rH) was passed through each tube at a rate of 1 L/min for 6 hours (equivalent to 1, 3 and 30 µg/m³ respectively). Front and back sections were extracted separately in acetonitrile. Extracts were analyzed by HPLC (Inertsil C18 column) with UV detection at 225 nm. Specificity was demonstrated by HPLC/DAD.

Results

See Table B.5.3-01. No interferences in the blanks and no breakthrough were observed. Mean recovery in quality control samples (tubes spiked with 0.36, 1.08 or 10.8 µg pyridaben, stored at ambient temperature and humidity without air flow) was 98%, 102% and 90% respectively. HPLC/DAD showed that the ratios of the pyridaben peak at 225 and 300 nm in an extract and the analytical standard were identical.

Conclusion

The method is suitable for the analysis of pyridaben in air with an LOQ of 1.0 µg/m³.

Remarks

1. Based on the AOEL of 0.002 mg/kg bw/day (see section B.6.10.5), the LOQ should be $0.3 \times 0.002 \text{ mg/m}^3 = 0.6 \text{ µg/m}^3$ or less (according to SANCO/825/00). The LOQ of the above method does not satisfy this requirement. However, the guidance in SANCO/825/00 is based on a daily respiratory volume of 20 m³ of a worker. In the toxicological section, the calculation of total respiratory volume of a worker is based on a respiration rate of 1.25 m³/hour and a working day of 8 hours, which gives a daily respiratory volume of 10 m³ of a worker. Based on the latter value, the LOQ should be 1.2 µg/m³ or less, and the LOQ of the above method satisfies this requirement.
2. Further information on specificity is not required since the methods for water and soil were highly specific.

Table B.5.3-01 Summary of method description and validation (soil, water and air).

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Soil 01 (pH 5.7, 2.6% OC, 94% sand ^(A))	Pyridaben	acetone/water (4:1), methanol/1N H ₃ PO ₃ (4:1)	C18 SPE clean-up, ENVL-Carb SPE clean-up	LC-MS/MS	0.01	0.01 0.1 0.5	83-95 (90) 74-93 (82) 90-94 (92)	5.5 (5) 9.7 (5) 1.6 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 02 (pH 6.1, 1.5% OC, 50% sand ^(A))	Pyridaben	As above	As above	LC-MS/MS	0.01	0.01 0.1 0.5	90-101 (95) 88-98 (92) 70-105 (87)	5.8 (5) 4.4 (5) 19 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 03 (pH 7.2, 2.4% OC, 31% sand ^(A))	Pyridaben	As above	As above	LC-MS/MS	0.01	0.01 0.1 0.5	82-89 (85) 70-95 (84) 88-104 (93)	3.2 (5) 14 (5) 7.2 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 04 (pH 8.2, 1.6% OC, 33% sand ^(A))	Pyridaben	As above	As above	LC-MS/MS	0.01	0.01 0.1 0.5	92-104 (99) 100-108 (103) 99-108 (104)	4.8 (5) 3.0 (5) 4.0 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 01 (pH 5.7, 2.6% OC, 94% sand ^(A))	P-14	As above	Centrifugation, filtration (45µm)	LC-MS	0.01	0.01 0.1 0.5	84-108 (94) 79-87 (83) 81-95 (88)	10 (5) 3.7 (5) 5.7 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 02 (pH 6.1, 1.5% OC, 50% sand ^(A))	P-14	As above	As above	LC-MS	0.01	0.01 0.1 0.5	84-96 (90) 79-104 (93) 99-105 (102)	5.0 (5) 9.7 (5) 2.2 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 03 (pH 7.2, 2.4% OC, 31% sand ^(A))	P-14	As above	As above	LC-MS	0.01	0.01 0.1 0.5	80-98 (87) 83-100 (93) 97-103 (100)	8.4 (5) 9.5 (5) 2.4 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 04 (pH 8.2, 1.6% OC, 33% sand ^(A))	P-14	As above	As above	LC-MS	0.01	0.01 0.1 0.5	93-104 (99) 92-101 (97) 90-105 (101)	4.1 (5) 3.6 (5) 6.2 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 01 (pH 5.7, 2.6% OC, 94% sand ^(A))	P-16	As above	As above	LC-MS	0.01	0.01 0.1 0.5	87-102 (95) 82-90 (85) 75-92 (87)	6.6 (5) 3.9 (5) 8.1 (5)	Yes	Tate S., 1993 (4.2.2/01)

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Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (mg/kg)	Recovery fortification level (mg/kg)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Soil 02 (pH 6.1, 1.5% OC, 50% sand ^(A))	P-16	As above	As above	LC-MS	0.01	0.01 0.1 0.5	86-98 (92) 87-102 (95) 91-102 (98)	5.0 (5) 6.4 (5) 4.3 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 03 (pH 7.2, 2.4% OC, 31% sand ^(A))	P-16	As above	As above	LC-MS	0.01	0.01 0.1 0.5	78-100 (88) 83-97 (91) 96-108 (100)	12 (5) 6.7 (5) 4.6 (5)	Yes	Tate S., 1993 (4.2.2/01)
Soil 04 (pH 8.2, 1.6% OC, 33% sand ^(A))	P-16	As above	As above	LC-MS	0.01	0.01 0.1 0.5	80-91 (87) 83-100 (92) 88-101 (95)	5.5 (5) 6.7 (5) 4.9 (5)	Yes	Tate S., 1993 (4.2.2/01)
Pond sediment	Pyridaben	methanol	Dichloromethane partition, Florisil column clean-up	GC-ECD	0.01	0.01 0.5	78-114 (91) 82-100 (88)	18 (4) 9.8 (4)	Yes	Delgado N., 1993 (4.2.3/01)
Ground water	Pyridaben	Dichloro- methane	C18 SPE clean-up	LC-MS/MS	0.005 µg/L	0.005 0.05	76-87 (80) 81-100 (92)	5.3 (5) 9.3 (5)	Yes	Tate S., 2002 (4.2.3/02)
Tap water	Pyridaben	As above	As above	LC-MS/MS	0.005 µg/L	0.005 0.05	71-100 (81) 75-110 (97)	14 (5) 16 (5)	Yes	Tate S., 2002 (4.2.3/02)
Surface water	Pyridaben	As above	As above	LC-MS/MS	0.005 µg/L	0.005 0.05	70-87 (75) 76-105 (90)	9.2 (5) 13 (5)	Yes	Tate S., 2002 (4.2.3/02)
Air (35°C, 80% rH)	Pyridaben	Tenax adsorbent is extracted with acetonitrile	Filtration	HPLC/UV	1 µg/m ³	1 3 30	100-109 (104) 91-98 (95) 85-92 (90)	3.0 (5) 3.1 (5) 3.5 (5)	Yes	Betteley J., 2001 (4.2.4/01)

(A) sand = 63-2000 µm particles.

Table B.5.4-01 Summary of method description and validation (blood).

Substrate	Analyte	Dissolution/ extraction	Partitioning/ clean-up	Quantifi- cation	Limit of quantifica- tion (µg/ml)	Recovery fortification level (µg/ml)	Recoveries % range (mean)	Repeatability RSD (%) (n)	Linearity demon- strated	Ref.
Blood	Pyridaben	acetonitrile/wate r (1:1)	C18 SPE clean-up	LC-MS/MS	0.05	0.05 0.5	95-100 (98) 88-93 (90)	2.2 (5) 2.1 (5)	Yes (0.025 – 2.5 µg/ml blood) r= 1.000	Tate, S., 2005 (4.2.5/01)

B.5.4 Analytical methods (residue) for body fluids and tissues (Annex IIA 4.2.5; Annex IIIA 5.2)

The notifier referred to the method described in study 7 and 8 (both GC-ECD), submitted under point B.5.2. This method however was not accepted as it used the very toxic methylating agent diazomethane. For body fluids and tissues only methods for the parent, pyridaben, are required. Therefore the use of diazomethane for derivatization is not required and the methods can be accepted for tissues.

STUDY 1**Characteristics**

Reference	: Tate, S., 2005 (IIA 4.2.5/01)	GLP statement	: Yes
Type of study	: Analytical methods in blood	Guidelines	: Incl. SANCO/825/00 rev.7
Year of execution	: 2005	Acceptability	: Acceptable
Test substance	: Pyridaben, lot no. 129S9006, purity 100.0%	Method reference	: Not indicated

Description of the method

1 ml of blood is extracted with 5 ml of acetonitril:water (1:1), dilution to 10 ml and cleanup-up of 1 ml with SPE (C₁₈), followed after drying of the eluate and reconstitution in 5 ml methanol/water/formic acid (50:50:1) by HPLC-MS/MS (20 µl injection volume, Phenomenex Luna C₈ column (15*2mm), positive electrospray, MRM 365>147 m/z for quantification and MRM 367>147 m/z for conformation).

Results

See table 5.4-01. No interferences in the blanks were observed.

Conclusion

The method is suitable for the analysis of pyridaben in blood with a LOQ of 0.05 mg/l.

Remarks

The LOQ was set on the lowest fortification level of 0.05 mg/l. However in the chromatograms (figures 7 and 8) the fortification levels were 0.1 and 1.0 µg/l. Notifier is asked to explain the differences.

B.5.5 Evaluation and assessment**Analytical methods for technical active substance and plant protection product**

A HPLC-UV method was submitted for the determination of pyridaben in technical material and in the plant protection product. This method was comparable to CIPAC method 583 for the determination of pyridaben in technical material and in wettable powders. The validation results fulfilled the criteria.

Analytical methods (residue) for plants, plant products, foodstuffs of plant and animal origin, feedingstuffs

Residue definition

The residue definition for post-registration monitoring and for risk assessment is proposed as pyridaben for tomato and citrus. No definition of residues in animal products was required, as no significant residues are expected in products of animal origin.

Orange fruit and orange process products

Three reports with validation data for GC-ECD method D9309 for the determination of pyridaben in orange and orange process products were submitted. The validation in the first report from 1994 supported an LOQ of 0.05 mg/kg for orange process products, but not for orange fruit. In orange whole fruit, accuracy and precision at 0.05 mg/kg did fulfil the criteria, but the residues in treated samples were corrected for apparent residues in untreated samples, which represented >30% of the claimed LOQ. The lowest validated level for orange fruit was therefore set to be 0.5 instead of 0.05 mg/kg. In the second report from 1994 this method was validated in orange fruit at an independent laboratory at 0.2 mg/kg. The validation in the third report from 2003 at again another laboratory confirmed an LOQ of 0.05 mg/kg for orange whole fruit and orange process products, and presented also a confirmatory technique (LC-MS/MS). The combined data support an LOQ (pre- and post-registration) of 0.05 mg/kg for orange fruit and orange process products (orange peel, orange oil, orange molasses, wet and dried orange pulp, orange juice, marmalade, canned orange).

Tomato

GC-ECD method D9312 for the determination of pyridaben was validated at 0.05 mg/kg in apple fruit and at 0.5 mg/kg in apple wet pomace (including an ILV for apple fruit and apple juice at 0.4 mg/kg). The same method was validated in another laboratory in tomato at 0.05 mg/kg. The validation provided in the first study for apple should also be relevant for tomato. Validation in tomato employed a HP-1 column (polarity comparable to DB-5), validation in another watery matrix, apple, employed a DB-17 column (medium polarity), whereas pyridaben residues in oranges determined by a DB-5 column could be confirmed with a DB-17 column. In addition, a LC-MS method is available for oranges. The combined data on selectivity indicate that the selectivity of the methods should be sufficient for tomato. The submitted data therefore support an LOQ (pre- and post-registration) of 0.05 mg/kg for tomato.

Other methods for plant products

Validation for another GC-ECD method (938/1) was submitted, which supported an LOQ of 0.05 mg/kg (pre-registration) for apples, pears, strawberry, tomatoes and peppers. The claimed LOQ of 0.05 mg/kg for orange fruit, grape and peach, that of 0.01 mg/kg for orange juice, and of 0.1 mg/kg for cotton seed were not accepted (interfering peak >30% LOQ and/or low replication in combination with high variability and/or accuracy outside 70-100% range). Method 938/1 is not accepted for post-registration since an attempt for validation in apple and peach at an independent laboratory at 0.05 mg/kg was not successful, and since no validation for a confirmatory method was provided.

Animal products

Validation was submitted for GC-ECD method D9405 for the determination of pyridaben and the metabolites PB-7 and PB-9 in animal products. This validation supported an LOQ of 0.01 mg/kg in milk and 0.05 mg/kg in fat, muscle, liver and kidney (including an ILV in liver), but a confirmatory method was not provided. Moreover, the method used the very toxic diazomethane as a methylating agent, which is not acceptable. Since no residues are expected in animal products, further questions are redundant.

Data requirements (methods for products of plant and animal origin)

The combined data for GC-ECD method D9309 support an LOQ (pre- and post-registration) of 0.05 mg/kg for orange fruit and orange process products (orange peel, orange oil, orange molasses, wet and dried orange pulp, orange juice, marmalade, canned orange). The combined data for GC-ECD method D9312 support an LOQ (pre- and post-registration) of 0.05 mg/kg for tomato.

Analytical methods for soil, water and air

Residue definition

Soil:	pyridaben, PB-22
Surface Water:	pyridaben, PB-7, W-1, B-3
Sediment:	pyridaben, PB-7
Ground water:	pyridaben, PB-4, PB-7, PB-22
Air:	pyridaben, PB-22, PB-7, B-3

Soil

Validation for the method to determine pyridaben and the metabolites PB-14 and PB-16 in soil supported an LOQ of 0.01 mg/kg for all three analytes. The method for P-14 and P-16 (LC-MS) is not sufficiently specific to be used for post-registration. The method for Pyridaben (tandem LC-MS/MS) is sufficiently specific.

Water

Validation for an LC-MS/MS method to determine pyridaben in water supported an LOQ of 0.005 µg/L in tap, ground and surface water. The LOQ of 0.005 µg/L for surface water is below the level of the lowest appropriate toxicity value for aquatic organisms (in this case the NOEC for daphnia (0.086 µg/L) (See B.9.2.3.1.2)).

Air

Validation for an HPLC-UV method to determine pyridaben in air supported an LOQ of 1 µg/m³. A confirmatory method is not required since the methods for water and soil were highly specific. The method is considered suitable for post-registration monitoring because the LOQ (1 µg/m³) is below the limit of 1.2 µg/m³ calculated using: limit = AOEL_{systemic} * 0.1 * 60/10 (based on a daily respiratory volume of a worker of 10 m³). The AOEL_{systemic} is 0.002 mg/kg bw/day (see section B.6.10.5).

Data requirements (methods for soil, water and air)

The methods for determination of pyridaben in soil, water and air are acceptable. Additional methodology for all the metabolites included in the residue definitions for water, soil and air should be submitted (data gap). If during review the residue definitions are modified, the data requirements for metabolites should be reconsidered.

Analytical methods (residue) for body fluids and tissues

As pyridaben is classified as toxic, methods validated in blood and tissues are required. The method submitted was that for the determination of pyridaben, PB-7 and PB-9 in animal products, which used a methylation step with diazomethane. The method excluding the methylation step is acceptable for pyridaben, except that a confirmatory method has not been provided.

Validation for a LC-MS/MS method to determine pyridaben in blood supported an LOQ of 0.05 mg/L. However there is a question for clarification of the fortification levels.

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B.5.6 References relied on**References for the active substance**

Annex point / reference number	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner
IIA, 4.1.1/01	Stanfield, K.C.	1991a	Validation of a Nissan Chemical Pyridaben technical assay method BASF Corporation Nissan Chemical Industries, Ltd. Report no. P52 GLP, Unpublished	Y	NCI
IIA, 4.1.1/02	Anonymous	1999a	Pyridaben 583: CIPAC method 1999, prepared by the Japanese Committee (JAPAC), chairman: N. Tamori, based on a method by Nissan Chemical Industries, Ltd. JAPAC, Japan Nissan Chemical Industries, Ltd. Report no. P30 GLP, Unpublished	N	-
IIA, 4.2.1/01	Tilting, N.	1991	GC method for the determination of Pyridaben in plants method no. 938/1 BASF Aktiengesellschaft Report no. R110 GLP, Unpublished	Y	BASF
IIA, 4.2.1/03	Abdel-Baky, S., Burkey, J. D., Malinsky, D. S.	1994	Method for determination of residues of Pyridaben in oranges and orange processed commodities by gas chromatography BASF Corporation BASF Aktiengesellschaft Report no. R112 GLP, Unpublished	Y	BASF
IIA, 4.2.1/04	Thiem, D. A.	1994	Independent laboratory method validation of BASF analytical method no. D9309 [Method for determination of residues of Pyridaben in oranges and orange processed commodities by gas chromatography] at Colorado Analytical Research and Development Corporation Colorado Analytical Research and Development Corporation BASF Aktiengesellschaft Report no, R113 GLP, Unpublished	Y	BASF
IIA, 4.2.1/05	Abdel-Baky, S.	1994	Method for determination of residues of Pyridaben in apple and apple processed commodities by gas chromatography BASF Corporation BASF Aktiengesellschaft Report no. R116 GLP, Unpublished	Y	BASF

Annex point / reference number	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner
IIA, 4.2.1/06	Perez, R., Griffin, P. A.	1994	Independent method validation of BASF analytical method no. D9312 "Method for determination of residues of Pyridaben in apples and apple processed commodities by gas chromatography" at Adpen Laboratories Adpen Laboratories, Inc. BASF Aktiengesellschaft Report no. R117 GLP, Unpublished	Y	BASF
IIA, 4.2.1/09	Tate, S.	2001	Pyridaben: Development and validation of methodology for the determination of residues of Pyridaben in tomatoes Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R150 GLP, Unpublished	Y	NCI
IIA, 4.2.1/10	Tate, S.	2003	Pyridaben: Validation of methodology for the determination of residues of pyridaben in oranges and orange processed commodities Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R303 GLP, Unpublished	Y	NCI
IIA, 4.2.1/11	-	1996	Analytical methods for pesticide residues in foodstuffs 6e edition June 1996 General inspectorate for health protection Ministry of Public Health, welfare and sports The Netherlands Published	N	-
IIA, 4.2.2	Tate, S.	2002a	Pyridaben: Development and validation of methodology for the determination of residues of Pyridaben and its two metabolites P-14 and P-16 in soil Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R31 GLP, Unpublished	Y	NCI
IIA, 4.2.3/01	Delgado, N.	1993	GC method for residue determination of Pyridaben (BAS 300 I) in pond sediment BASF Corporation BASF Aktiengesellschaft Report no. F4 GLP, Unpublished	Y	BASF
IIA, 4.2.3/02	Tate, S.	2002b	Pyridaben: Validation of methodology for the determination of residues of Pyridaben in ground, tap and surface water Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R35 GLP, Unpublished	Y	NCI

Annex point / reference number	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner
IIA, 4.2.4	Betteley, J.M.T.	2001	Pyridaben: Development and validation of a method of analysis in air Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R40 GLP, Unpublished	Y	NCI
IIA, 4.2.5/01	Tate, S.	2005	Pyridaben: validation of methodology for the determination of residues of pyridaben in blood Huntingdon Life Sciences Ltd. Nissan Chemical Industries, Ltd. Report no. R45 25 th August 2005 GLP, Unpublished	Y	NCI
IIA, 4.2.5/02	Abdel-Baky, S., Malinsky, D. S.	1995	Method for determination of residues of Pyridaben (PB-1, PB-7, and PB-9) in animal tissues (fat, muscle, liver and kidney) and milk by gas chromatography BASF Corporation BASF Aktiengesellschaft Report no. R118 GLP, Unpublished	Y	BASF

References for the plant protection product

Annex point / reference number	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner
IIIA, 5.1.1/01	Anonymous	1999b	Pyridaben 583: CIPAC method 1999, prepared by the Japanese Committee (JAPAC), chairman: N. Tamori, based on a method by Nissan Chemical Industries, Ltd. JAPAC, Japan Nissan Chemical Industries, Ltd. Report no. P30 GLP, Unpublished	N	-
IIIA, 5.1.1/03	Stanfield, K.C.	1991b	Validation of a Nissan Chemical Pyridaben formulated product assay method BASF Corporation BASF Aktiengesellschaft Report no. P54 GLP, Unpublished	Y	BASF